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PNEUMONIA IN HOSPITAL PRACTICE

By Neville C. Oswald, G. Simon and R. A. Shooter

St. Bartholomew's Hospital, London

Recent advances in the treatment of pneumonia have been spectacular, and the introduction of sulphonamides and antibiotics has been accompanied by a fall in the death rate from approximately 30 per cent. to 10 per cent. in the last 25 years. During this period reports of personally observed series have appeared in the British literature from time to time, and the efficiency of these drugs has been amply confirmed (Humphrey *et al.*, 1948; Crofton *et al.*, 1951; Grist *et al.*, 1952; Stuart-Harris, 1953). Yet pneumonia is still a common and serious disease. From the evidence of death certificates, it causes roughly 20,000 fatalities each year, which is 4 per cent. of deaths from all causes or 50 per 100,000 of the population. There are several reasons for these continuing high mortality figures.

The purpose of this communication is to review pneumonia as it has presented at a large general hospital during the past decade, with a view to assessing outstanding problems in the light of recent therapeutic advances.

Material and Methods

The records of all patients admitted to St. Bartholomew's Hospital with acute respiratory disease, who on discharge were considered to have had "clinical" pneumonia in the period 1949 to 1958, have been reviewed. Some were found later to be suffering from pulmonary tuberculosis or bronchial carcinoma, and others had been transferred from other hospitals for the treatment of complications such as lung abscess or empyema: these have all been excluded. There remained 1,330 patients who were either admitted direct to hospital or were referred by general practitioners. The pneumonia or its complications appeared to be the precipitating cause of the clinical state in each case. No account has been taken of pneumonia developing after admission.

Bacteriology

Sputum was examined by the same method throughout. After inspection, thin and thick films were prepared from purulent portions and were stained by Gram and Ziehl-Neelsen stains respectively. Cultures were made on horse blood agar plates, after preliminary rinsing of the inoculum in a tube of saline to wash off mouth bacteria.

Although the antibiotics used in testing sensitivity varied, the method was not changed. Before inoculation, cups were cut with a cork borer from plates on which the primary cultures were made, and the holes so made were filled with antibiotic. Amongst other advantages, this method made possible the despatch of the report on the day after receipt of the specimen. It is not easy to

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ensure that every specimen labelled "sputum" has come from the chest. Gross contamination with mouth cells and bacteria can occur, and some specimens appeared to consist of little more than saliva. Throughout the period the practice in the laboratory was to endeavour to examine genuine sputum only. If macroscopic or microscopic examination suggested an origin in the mouth, an attempt was made to obtain another specimen.

Radiology

The custom of the hospital is to discard normal radiographs of the chest after two years and abnormal films after five years, unless their retention is requested, or the patients are continuing to attend. Hence the radiographic analysis in this series is confined to the years 1954-58. During this period 752 patients were admitted with pneumonia, of whom 654 (87 per cent.) had a radiograph of the chest. A shadow consistent with pneumonia was seen in only 541. The discrepancy arose from several causes. Sometimes the films were taken too long after the onset of the infection, or after the institution of chemotherapy, or in some instances fresh consolidation could not be distinguished from pre-existing abnormal shadows; in others the radiographic technique was faulty. In yet other cases the absence of radiological evidence had been overruled when the clinical diagnosis was made.

Results

Of the 1,330 patients, 861 were males and 469 were females. Their age distribution is shown in Table I. Little importance can be attached to the proportion of children (23 per cent. under the age of 15), which is influenced by the availability of beds in the children's wards. Of more significance are the

Table I.—Age Distribution and Mortality of 1,330 Patients admitted to Hospital with Pneumonia

	-4	5-	15-	25-	35-	45-	55-	65-	75-	Total
Number	160	143	72	94	126	186	272	194	83	1,330
Deaths	11	0	0	2	2	14	22	39	19	109
Percentage mortality ..	6·9	0	0	2·1	1·6	7·5	8·1	20·1	22·9	8·2

relatively large figures for admission after the age of 45. This is partly accounted for by pre-existing chronic diseases, particularly chronic bronchitis and emphysema which often determined the need for hospital care, and partly by the frailty of the very old, in whom pneumonia is often serious.

Causes of Death

In considering the causes of death, four outstanding contributory causes were apparent, namely age, clinical state on admission, pre-existing chronic diseases and uncontrolled pneumonic infection.

(*a*) *Adults* (98 fatalities).

(i) Fifty-eight (59 per cent.) of the patients who died were aged 65 or more and 19 (19 per cent.) were at least 75 years old. Whatever associated diseases they may have had, many seemed to be too frail to withstand a serious illness.

(ii) Thirty-four (35 per cent.) were judged to have been moribund on admission and only survived a few hours or days despite resuscitation; 19 of these were aged 65 or more. The gravity of the illness, often with coma, cachexia or malnutrition, was such that treatment was ineffective.

(iii) Twenty-five (25 per cent.) patients were under the age of 65 and were not moribund on admission: the principal causes of death seemed to be uncontrolled pneumonic infection (7), chronic bronchitis and emphysema (6), heart disease (6), pulmonary embolism (2), cerebral thrombosis (2), anuria (1) and staphylococcal enteritis (1).

(*b*) *Children* (11 fatalities).

All but two of the deaths occurred in babies under the age of 9 months. The causes of death were uncontrolled fulminating infections (6), cystic fibrosis of the pancreas (2), congenital hydronephrosis (1), congenital hypothermia (1) and pyelonephritis (1).

Pre-existing Associated Diseases

No less than 634 (63 per cent.) of the adult patients suffered from pre-existing diseases, the most important of which are listed in Table II. As respiratory disorders were so much commoner than the others, the adults were divided into four groups according to pre-existing diseases as follows: (1) none, (2) non-respiratory, (3) respiratory, (4) respiratory and non-respiratory.

Table II.—Principal Associated Diseases in 1,027 Adult Patients admitted to Hospital with Pneumonia

Respiratory		*Non-respiratory*	
Bronchitis and emphysema	386	Heart disease	125
Asthma	43	Neurological	35
Bronchiectasis	24	Blood diseases	30
Recurrent pneumonia	12	Diabetes	29
		Digestive disorders	27
Other respiratory	11	Skeletal deformities	16

Influence of Pre-existing Diseases upon Complications and Mortality

Adults: Table III shows that pre-existing respiratory and non-respiratory diseases seemed to have little effect upon the incidence of pleural effusion, lung abscess or delayed resolution (persistence of radiological consolidation for a month or more after the onset of pneumonia).

The death rate was only 5 per cent. in otherwise normal patients, but rose to 23 per cent. in patients with both respiratory and non-respiratory chronic diseases. Of the associated chronic diseases, 60 were respiratory (bronchitis and emphysema 52, bronchiectasis 4, asthma 2, recurrent pneumonia 2)

and 24 were cardiovascular (ischæmia 12, hypertension 9, others 3), see Table V, which together accounted for over three-quarters of the total. Amongst the others were diseases of the central nervous system (6), diabetes (4), cancer (3), rheumatoid arthritis (3) and cirrhosis of the liver (2).

Children: Pleural effusion, lung abscess and delayed resolution were all much less common than in older patients (Table III). Associated diseases were also less frequent, being found in 90, or 30 per cent., compared with 63 per cent.

TABLE III.—PULMONARY COMPLICATIONS AND MORTALITY RATES IN 1,330 PATIENTS ADMITTED TO HOSPITAL WITH PNEUMONIA, ACCORDING TO ASSOCIATED DISEASES

	Total	*Pleural effusion* No. %	*Abscess* No. %	*Delayed resolution* No. %	*Death* No. %
Age 15 or more					
Associated disease:					
None	393	43 11	30 8	59 15	19 5
Non-respiratory	158	25 16	11 7	7 4	19 12
Respiratory	372	29 8	21 6	38 10	36 10
Respiratory and non-respiratory	104	9 9	7 7	5 5	24 23
Aged under 15	303	4 1	7 2	3 1	11 4
Totals	1,330	110* 8	76 6	112 8	109 8

* Included 22 (1·7 per cent.) empyemata.

in adults. Again, respiratory complaints formed more than half of the total (asthma 22, bronchitis 20, bronchiectasis 9, recurrent pneumonia 5). In the non-respiratory group, diseases of the central nervous system (12), congenital heart disease (8) and blood disorders (4) occurred most frequently.

CHRONIC BRONCHITIS AND EMPHYSEMA

The age distribution of the 386 (38 per cent.) patients in whom this diagnosis was made is shown in Table IV. The percentages rise until they reach the sixth decade, when they continue at about 50 per cent. The overall mortality rate in the bronchitic patients was 14 per cent. The figures in the age groups 25-54 exceed those for the whole series (see Table I), after which they are substantially similar.

CARDIOVASCULAR DISEASE

Table V shows the age distribution and mortality of 125 patients with pre-existing cardiovascular disease. Hypertension was defined as systolic blood pressure of more than 200 mm. Hg or a diastolic pressure of more than 100 mm. Hg. Most of the " other " patients had congenital heart disease. Ischæmia and hypertension were associated with mortality rates well in excess of those for the whole series, but of the 22 deaths, 12 occurred in patients aged 70 or more.

TABLE IV.—AGE DISTRIBUTION AND MORTALITY RATES OF 386 ADULT BRONCHITIC PATIENTS WITH PNEUMONIA

Age	*All patients*	*Patients with chronic bronchitis*			
		No.	*Per cent. of all patients*	*Deaths*	*Deaths as per cent.*
15-	72	10	14	—	—
25-	94	9	11	1	11
35-	126	26	21	1	4
45-	186	59	32	9	15
55-	272	142	52	14	10
65-	194	99	51	19	19
75-	83	41	49	8	20
Total ..	1,027	386	38	52	14

OTHER CHRONIC DISEASES

Of the remaining chronic diseases listed in Table II, respiratory affections other than chronic bronchitis and emphysema existed in 8 of the fatal cases and disorders of the central nervous system, particularly hemiplegia, in 6. Of the 29 diabetics, 4 died but the diabetes remained uncontrolled in only one of these. Cancer, rheumatoid arthritis and cirrhosis of the liver were present in others.

TABLE V.—MORTALITY IN 125 PATIENTS WITH PRE-EXISTING CARDIOVASCULAR DISEASE

	All patients	*Deaths*		*Total deaths*	*Percentage deaths*
		Under 70	*70 or more*		
Ischæmia ..	51	4	9	13	26
Hypertension ..	37	5	3	8	22
Rheumatism ..	23	1	—	1	4
Others ..	14	—	—	—	—
Total	125	10	12	22	18

BACTERIOLOGY

Sputum was examined from 809 of the 1,330 patients within 4 days of admission to hospital. The relatively low figure is partly accounted for by the inclusion of 303 children, only 41 of whom had sputum examined.

In Table VI the patients are classified by their associated diseases and by the bacteria isolated from the sputum. The heading " no pathogens " in the last column refers to cultures which consisted chiefly of mixed growths of organisms

derived from the mouth or were sterile; they comprised 40-50 per cent. of specimens in each groups. The patients shown in this column included many (rather less than 20 per cent. of the whole series) to whom antibacterial drugs had been given before admission. There remained 443 patients in whose sputa

TABLE VI.—BACTERIOLOGY BY ASSOCIATED DISEASES
(Omitting cases with no specimen)

	Total	*Strep. pneumoniæ*		*H. inf.*		*Staph. aureus*		*Strep. pyogenes*	*Friedländer*	*Others*	*No pathogens*	
		No.	%	*No.*	%	*No.*	%	*No.*	*No.*	*No.*	*No.*	%
Age 15 or more Associated disease:												
None	286	87	30	49	17	21	7	6	1	5	143	50
Non-respiratory	96	28	29	20	21	4	4	2	—	—	48	50
Respiratory ..	301	103	34	109	36	7	2	6	3	3	119	40
Respiratory and non-respiratory	85	25	29	32	38	4	5	—	1	—	36	42
Aged under 15	41	12	29	10	24	3	8	2	—	—	20	49

Note: Specimens from which more than one pathogenic organisms were isolated are counted in each appropriate column.

pathogenic bacteria were found. The most striking finding in the table is the increased frequency with which *H. influenzæ* was isolated from patients with associated respiratory diseases. Lobar pneumonia resembling that caused by the pneumococci has been attributed to this organism, but no certain instance of it was seen in this series. Twenty of the patients had a confluent pneumonia involving at least half a lobe, with *H. influenzæ* in the sputum, but 19 of these either had some other potential pathogen as well or had had chemotherapy before admission. Another feature to be noted is the even distribution of *Strep. pneumoniæ* between the groups, the percentages all falling within the range 29-34. In children, the incidence of pathogenic bacteria was similar to that in adults who had no pre-existing respiratory diseases.

The death rate was lowest—3·7 per cent.—for the 162 patients having a pneumococcus as the sole pathogen in the sputum; of the 6 deaths, 4 occurred in patients with associated diseases, the remaining two succumbing to pulmonary embolism and cerebral thrombosis respectively. Altogether, the pneumococcus was isolated from 255 patients, of whom 13 (5·1 per cent.) died. Of the 220 patients having *H. influenzæ* in the sputum, 21 (9·6 per cent.) died, of whom 13 had chronic bronchitis. Three of the 39 (7·7 per cent.) patients with staphylococcal pneumonia died, one of whom had hypertension and uræmia in addition, and the other two chronic bronchitis. Friedländer's bacillus was isolated from 5 patients, of whom 2 died; one was moribund on admission and died 6 hours later and the other developed a fatal pyelonephritis.

Radiology

The shadows were classified according to extent and also into those which were predominantly homogeneous (68 per cent.) and those which were mottled and consisted of very small ill-defined areas of clouding (32 per cent.).

Table VII shows that the consolidation was more often basal than in the

Table VII.—Distribution of Radiological Consolidation by Lobes

	Upper	*Middle*	*Lower*
Right ..	91	95	212
Left ..	36	18	186
Total ..	127	113	398

Note: Patients with two shadows, or with shadows extending over two lobes, are counted twice in this table.

upper parts of the lung; it was homogeneous rather than mottled, but was often mottled when less than one bronchopulmonary segment was involved (Table VIII).

Table VIII.—Size and Type of Radiological Consolidation

Extent	*Total*	*Homogeneous*	*Mottled*
Less than 1 segment ..	182	98 (54%)	84 (46%)
1 segment	131	106 (81%)	25 (19%)
2 sep. segments ..	38	27 (71%)	11 (29%)
Half a lobe	63	45 (71%)	18 (29%)
More than half a lobe ..	127	92 (72%)	35 (28%)
Total ..	541	368 (68%)	173 (32%)

In Table IX the type and extent of radiological shadows are related to age. With increasing years homogeneous opacities tended to become less frequent and mottling more frequent. In seeking an explanation for this trend, radiographs of the age group 35-64 were studied for evidence of emphysema. The radiological signs of emphysema were taken to be a low and flat diaphragm, a large main pulmonary trunk and prominent hilar vessels with small intrapulmonary vessels, and bullæ or bullous areas (Simon, 1958). If two or more of these were present a diagnosis of emphysema was made. The table shows that radiographs without evidence of emphysema still had a clear predominance of homogeneous shadowing due to the pneumonia, similar to that in the younger age groups, whereas those with additional X-ray evidence of emphysema showed mainly the mottled type of pneumonic shadow.

The extent of radiological shadowing did not vary much with age, although the older and emphysematous patients tended to have a higher proportion of small opacities, and therefore of mottled shadows (Table VIII). In some cases the consolidation was patchy if perhaps there was no exudate into the bullæ.

TABLE IX.—TYPE AND EXTENT OF RADIOLOGICAL CONSOLIDATION COMPARED WITH AGE, EMPHYSEMA AND DEATHS

	Total number	*Number with shadow* %		*Extent of shadow** %		
		Homo.	*Mottled*	*Large*	*Medium*	*Small*
Age						
0-14	92	80	20	37	34	29
15-34	76	78	22	34	34	32
35-64	47	65	35	34	33	34
65 and over ..	126	60	40	38	24	38
Age 35-65 only						
Emphysema ..	65	40	60	31	27	42
No emphysema ..	182	74	26	34	35	31
Deaths	50	51	49	61	15	24

* "Large" = lobar or half lobar.
"Medium" = segmental (including two separate segments).
"Small" = less than 1 segment.

Films were available for only 30 of the patients who died and in these the distribution between homogeneous and mottled shadows was unremarkable. A high proportion had large areas of opacity.

Discussion

The factors which adversely affect the prognosis of pneumonia include old age, pre-existing chronic diseases and inadequate or delayed treatment.

The mortality rate for pneumonia in series from British hospitals has been fairly constant in recent years, being 5 per cent. in a series with 12 per cent. of the patients aged 60 or more (Humphrey *et al.*, 1948), 7 per cent. in one with 25 per cent. of patients aged 60 or more (Antibiotics Clinical Trials Committee, 1951), 9 per cent. (Crofton *et al.*, 1951), and in this series 8·2 per cent. with 21 per cent. of the patients aged 65 or more. Humphrey *et al.* (1948) comment that deaths mainly occurred with massive infection in the elderly who had been ill for several days before admission. In the series of the Antibiotics Clinical Trials Committee (1951), 12 of the 19 deaths occurred in patients aged 60 or more; and of 19 patients who were "desperately ill on admission," 10 died. Crofton *et al.* (1951) noted that 8 of the 10 deaths occurred in patients over the age of 60. In our experience, 59 per cent. of the adult patients who died were aged 65 or more and 35 per cent. were judged to have been moribund on admission.

Occasional reference has been made to pre-existing chronic diseases. Thus, Humphrey *et al.* (1948) found that 43 per cent. of their patients gave a history of previous pneumonia or chronic bronchitis. Chronic bronchitis was noted in 17 of 19 fatalities by the Antibiotics Clinical Trials Committee (1951) and in 5 of the 10 deaths by Crofton *et al.* (1951). The occurrence of bronchitis in 38 per cent. of all adults and in 52 per cent. of the deaths in this series places this diagnosis far above the others. Cardiovascular disease was shown in 12 per cent. of the adults and in 22 per cent. of those who died. These figures would probably have been larger if more detailed tests, such as electrocardiograms, had been performed routinely, particularly in the elderly. Some of the bronchitic deaths might also more properly be described as cardio-respiratory deaths.

From the bacteriological standpoint, the pneumococcus remains the most commonly isolated pathogen, but its isolation from only 31 per cent. of patients from whom a satisfactory specimen of sputum was obtained, whilst being similar to the experience of Crofton *et al.* (1951) who found it in 26 per cent., is far lower than was usual when accessory methods of isolation were practised and antibiotics were not available to patients before they were admitted to hospital. It was found with equal frequency in otherwise healthy adults, chronic bronchitics and children, suggesting that neither age nor associated chronic respiratory disease should influence the choice of antibiotic for routine treatment. Every effort must be made to obtain specimens before chemotherapy is started, and the rapid detection of such organisms as *Staph. aureus* and Friedländer's bacillus may be life saving. Reviewing the 109 deaths, 13 appeared to be due primarily to uncontrolled bacterial infection with, according to the evidence of the radiographs, unusually extensive pulmonary consolidation. Of the 13, 6 were infants; pathogenic bacteria were found in 6 (pneumococcus 2, *Staph. aureus* 2, Friedländer's bacillus 2), and another 4 succumbed to fulminating influenza. Some of these deaths might have been avoided by earlier and adequate chemotherapy.

Some aspects of the bacteriology of pneumonia in chronic bronchitis and of the radiology of pneumonia in emphysema have emerged from this study. *H. influenzæ* was isolated from the sputum of 37 per cent. of patients with previous chronic respiratory disease and of only 19 per cent. of those with previously healthy lungs. Whilst no proof exists that the common non-encapsulated *H. influenzæ* of chronic bronchitics plays a significant part in the pneumonic process, it is likely to contribute to the associated acute bronchitis. Perhaps this should be remembered when the choice of an appropriate antibiotic is being considered. A study of the radiographs in this series shows a clear trend towards mottled consolidation when emphysema is present, due partly to failure of the air spaces in the lungs to consolidate.

Summary

1. The records of all patients admitted to St. Bartholomew's Hospital with a diagnosis of pneumonia or its complications during the period 1949-58 have been reviewed. Of the 1,330 patients, 861 were males and 469 females; 303 were children under the age of 15.

2. Some 634 (63 per cent.) of the adults and 90 (30 per cent.) of the children had a pre-existing disease. Respiratory disorders, particularly chronic bronchitis and emphysema, and cardiovascular diseases were by far the commonest concomitants.

3. There were 109 (8·2 per cent.) deaths, 98 in adults and 11 in children. Of the adults, 59 per cent. were aged 65 or more and 35 per cent. were judged to have been moribund on admission; of the 25 per cent. who were under the age of 65 and were not moribund on admission, uncontrolled pneumonic infection, chronic bronchitis and emphysema, and heart disease, seemed to be the principal causes of death. Of the 11 fatalities in childhood, 6 were attributed to uncontrolled fulminating infections.

4. Bronchitis was diagnosed in 38 per cent. of the adults and 52 per cent. of the patients who died. Cardiovascular disease existed in 12 per cent. of the adults and 22 per cent. of the deaths.

5. The pneumococcus was found with equal frequency in the sputum of otherwise healthy adults, chronic bronchitics and children. *H. influenzæ* was found twice as often in patients with pre-existing chronic respiratory diseases as in those with previously healthy lungs.

6. Homogeneous radiological consolidation was twice as common as mottling, but mottling became relatively more frequent with advancing years. This trend can be accounted for to a large extent by emphysema, in which the opacities were predominantly mottled.

7. In children, associated diseases and pulmonary complications were less common than in adults, but the mortality was high in infancy. The bacteriology of the sputum and the radiological appearances were similar to those seen in adults who did not have chronic respiratory diseases.

Our sincere thanks are due to the physicians of the hospital for allowing us to review their patients. We are also most indebted to Mr. N. P. Curwen, medical statistician, Miss E. J. Armour and other members of the Department of Medical Statistics for their assistance with the tables.

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RESULTS AND COMPLICATIONS OF PULMONARY RESECTION IN THE TREATMENT OF TUBERCULOSIS*

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The number of operations in the treatment of pulmonary tuberculosis in Poland is about 3,000 annually (Rzepecki, 1959). The majority of the resections included in this number have been done in this clinic, so that our material is representative for Poland.

The number of resections in recent years has gradually increased at the expense of collapse operations. At present, resections constitute more than 90 per cent. of the total. In March 1960 the number of resections reached 1,500. The first operation of this type carried out in Zakopane was performed in 1948.

Temporary phrenic paralysis has been abandoned altogether and only three adhesion sections have been done in the past year. Only ten patients have had an extrapleural pneumothorax this year. Monaldi drainage, speleotomy and plombage with plastic materials have also been given up; decortication unaccompanied by resection is now seldom done.

A large number of the operations were done before the advent of antibiotics or before their proper use was known. The indications for collapse operations and for resections have been different, and for these reasons a comparison of the results of the procedures has been impossible. Table I, however, gives the results of the three operations in this clinic. (Błędowska, 1958; Langer and Lewandowska, 1959).

Table I.—Mortality and Complications of Resection, Thoracoplasty and Extrapleural Pneumothorax

Early results = 4 months

Operation	*Mortality* %	*Bronchial fistula* %	*Empyema* %	*Exacerbation and spread* %	*Mortality after (Eerland, 1955)* %
Resection, 1,077 1948-58	3·4	7·2	4·8	3·2	2·0
Thoracoplasty, 711 1946-56	3·6	0·56	4·7	5·1	5·5
Extrapleural pneumothorax, 980 1946-56	0·8	0·8	6·75	5·2	3·3

* Delivered as a lecture at the 11th International Course of Pulmonary Resection, held in Zakopane June 1960.

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The low mortality up to three months after extrapleural pneumothorax of only 0·8 per cent. is striking; so is the relatively high incidence of empyema. On the other hand, in resections the incidence of bronchopleural fistulæ was high.

The causes of death in the 46 patients are shown in Table II.

TABLE II.—CAUSE OF DEATH IN 1,341 OPERATIONS

Cause	*Number of cases*	*Per cent.*
Bronchial fistula	13	1
Shock	6	0·5
Pulmonary arterial embolism	6	0·5
Cardiac and/or respiratory failure ..	5	0·4
Exacerbations of tuberculosis	3	0·2
Anæsthetic cause, suicide, cause unknown, hæmorrhage at 2 cases	8	0·6
Broncho-œsophageal fistula, hæmorrhage, pneumonia, hæmorrhagic diathesis, pneumothorax at 1 case	5	0·4
Total	46	3·6

46/1,270 patients = 3·6 per cent.

Operative and post-operative shock was the cause of death of 6 patients, two of whom had irreversible cardiac arrest. Deep thrombophlebitis of the lower extremity followed by pulmonary embolism was the cause of death in 6 patients. Five patients were lost from cardio-respiratory failure, and three from relapse of progressive tuberculosis. Specific exacerbations during the patient's stay in the sanatorium were frequently associated with drug resistance.

In two patients death was due to suicidal jump from a window. A slip of the ligature of the inferior vein was the cause of death in a young woman, and hæmorrhage from the pulmonary artery in another patient. Bronchopneumonia caused the death of one patient after a one-stage bilateral resection. Nephrosis occurred following a pneumonectomy, after completion of a course of viomycin, but it could not be attributed to this drug. Hæmorrhagic diathesis caused a hæmorrhage into the fourth ventricle resulting in the death of one patient. Pneumothorax with collapse of a residual lobe was another fatal complication.

OPERATIVE COMPLICATIONS

The most frequent accident at operation was *cavity rupture* (Table III). In the era of collapse therapy this was usually fatal, but now, when resections are done under adequate antibiotic cover, the accident has practically lost its importance.

A more severe complication which often led to respiratory insufficiency was accidental injury to the phrenic nerve. This occurred more frequently on the left side, usually during the division of dense adhesions in decortication.

TABLE III.—OPERATIVE COMPLICATIONS OF 1,341 LUNG RESECTIONS IN TUBERCULOSIS

No.	*Kind of complications*	*Number of cases*	*Per cent.*
1	Rupture of cavity	159	12
2	Damage to phrenic nerve	42	3
3	Hæmorrhage from pulmonary artery ..	36	2·5
4	Shock	18	1·5
5	Damage to diaphragm	17	1·5
6	Hæmorrhage from pulmonary vein ..	13	1·0
7	Damage to bronchus	8	0·5
8	Opening of pericardium	8	0·5
9	Damage to vagus nerve	6	0·4
10	Damage to recurrent nerve	5	0·5
11	Damage to sympathetic nerve	3	0·2
	Total	315	23·5

Hæmorrhage from the pulmonary artery occurred more often on the left side, but in only a few cases was it necessary to extend the planned resection. In most, suture of the walls of the artery was possible.

The other complications listed were those which might normally be expected to occur in a series of this size.

LATE SPECIFIC COMPLICATIONS

An increase in the incidence of streptomycin resistance of the organisms found in surgical patients has occurred (Lewandowska, 1960). At present, every fourth patient has to have drugs other than streptomycin during the operative period, and the incidence of INAH resistance in our clinic has reached 73 per cent. during the last year (Fig. 1).

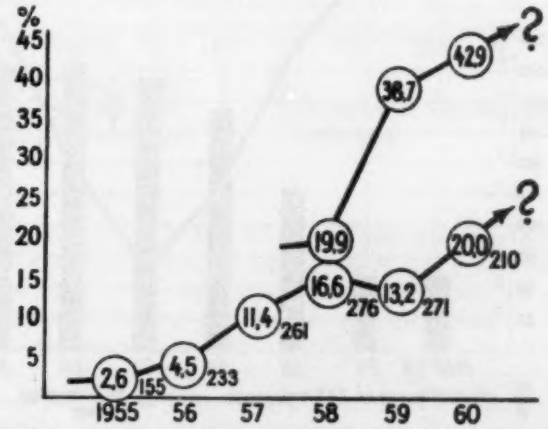

FIG. 1. The incidence of resistance to streptomycin is shown as the lower line; that to P.A.S. as the upper line.

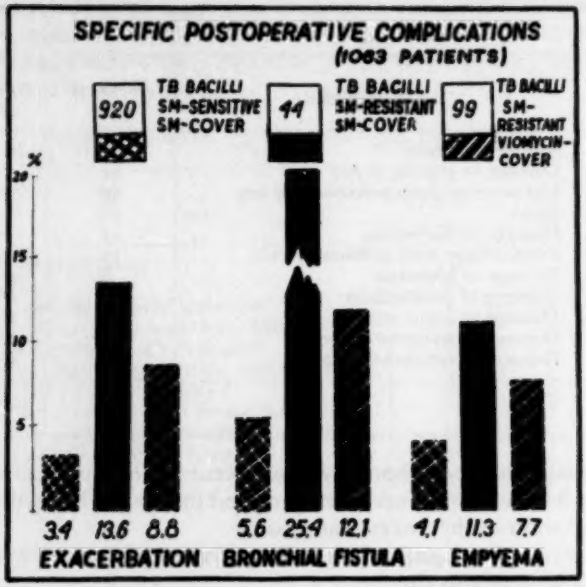

FIG. 2. The figures at the foot of each column represent the percentage incidence indicated by the respective column.

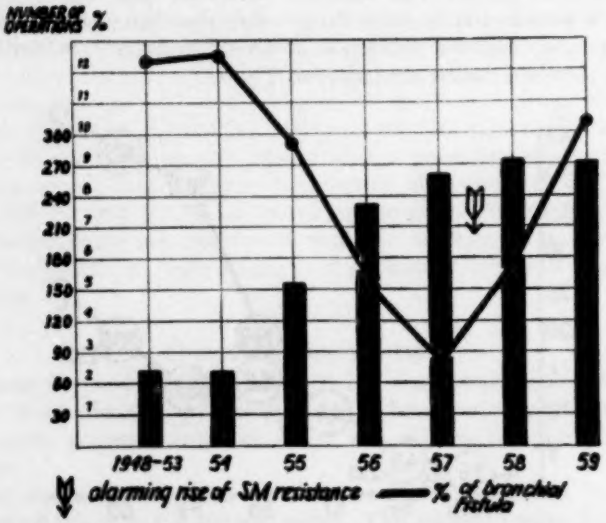

FIG. 3. The heavy columns indicate the number of operations done each year: the thin line indicates the percentage incidence of bronchopleural fistulas.

The incidence of specific complications such as bronchopleural fistula, empyema and the spread of the infection was highest in the streptomycin resistant group (Fig. 2) and lowest in the patients with streptomycin sensitive organisms. Although viomycin reduced the incidence of these complications significantly, it was found to be inferior to streptomycin, which was the least toxic and the most effective drug.

In 1957 the incidence of bronchopleural fistula had dropped to 2·7 per cent., but it has since increased to 10·3 per cent. (Fig. 3). This has been the result of the growing incidence of drug resistance. The frequency of this complication has lessened in the last year since the introduction of pyrazinamide, cycloserin and 1314 T.H.

There was a high incidence of fistulæ after segmental resection. The tendency to conserve pulmonary tissue may have undesirable effects. It is better to sacrifice a doubtful third segment than to preserve it at the cost of a bronchopleural fistula.

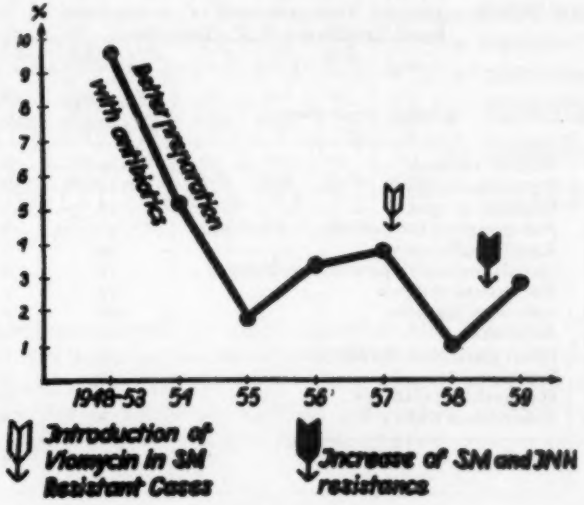

FIG. 4.

Fig. 4 shows the frequency of post-operative exacerbations during the last twelve years and also the effect of the antibiotics on this type of complication. A progressive decrease in the number of exacerbations is seen up to 1955; after this there was an increase, but this was combated by the use of viomycin and by more prolonged post-operative chemotherapy. The continued upward trend was due to an increase in the incidence of resistant organisms, and in the past year no less than seven patients had post-operative exacerbations. All had INAH resistant bacilli and were receiving this drug only, before their operation.

All three specific complications were frequent when pulmonary tissue containing tuberculous lesions was transgressed at operation (Rzepecki, 1960).

We have tried to find an explanation of this phenomenon in incorrect chemotherapy. Paryski and others (1960) found a high incidence of viable bacilli (57 per cent.) in encapsulated lesions in resected lung tissue. This cannot therefore be operated upon with impunity.

Non-specific Complications (Table IV)

Non-specific wound infections including stitch abscesses were not found by Lewandowska (1959) to be commoner in patients unprotected by antibiotics. Penicillin resistant staphylococci are endemic in this clinic, and in cases of wound infection other antibiotics such as terramycin were used. There were no deaths due to wound infection so the complication was not an important hazard.

Table IV.—Non-specific Post-operative Complications in 1,341 Lung Resections in Tuberculosis

No.	*Kind of complication*	*Number of cases*	*Per cent.*
1	Wound infection	114	8·5
2	Thrombophlebitis	111	8·5
3	Residual air space	43	3
4	Post-operative hæmorrhage > 2,000 ml.	42	3
5	Renal insufficiency	39	3
6	Circulatory and respiratory insufficiency ..	32	2·5
7	Post-operative shock	27	2
8	Infectious hepatitis	27	2
9	Atelectasis	20	1·5
10	Heart asystole or fibrillation	13	1
11	Psychosis	9	0·5
12	Hæmorrhagic diathesis	3	0·2
13	Tuberculous iridocyclitis	1	0·1
	Total	481	35·2

Thrombophlebitis either in deep or superficial veins was found to be commoner in patients with respiratory insufficiency. It was uncommon, but in two patients it was complicated by pulmonary embolism.

Persistence of an apical pocket of air was not found to be a serious complication. There were 43 such cases in this series and on occasions a limited thoracoplasty had to be carried out to obliterate the space.

Post-operative bleeding, when severe (more than 2 litres in the first five hours after operation), was treated by thoracotomy. It was usually possible to find the bleeding point which was often an intersegmental vein. There were no deaths in this group.

Bilateral Operations

In all, forty-two bilateral operations were done either in one or two stages. Patients in the younger age groups with circumscribed lesions were chosen. The respiratory function was carefully assessed before operation, and the chemotherapy had to be flawless (Rzepecki, 1959).

Among the one-stage operations, bilateral apico-posterior segmentectomies predominated (Fig. 5). The two-stage operations included one patient who had

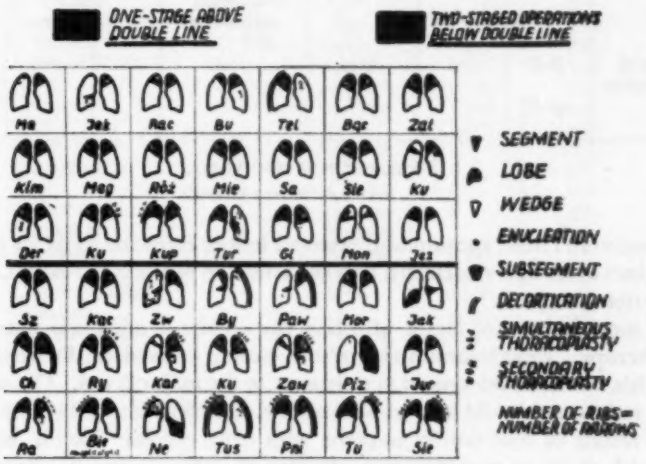

FIG. 5.

bilateral lobectomy involving eight segments and bilateral thoracoplasty. One woman had had a partial resection of the second lung after a pneumonectomy (Rzepecki, 1960). She did well. There were three deaths after bilateral resection; two due to pulmonary emboli, and one due to bronchopneumonia. Only one of the survivors remained sputum-positive.

Late Results

The late results of the three operations are shown in Table V. The sputum conversion rate is similar in all three groups (more than 90 per cent., in each), and almost nine out of ten patients in each group have been able to return to work.

Discussion

Pulmonary resection in tuberculosis and the results of this type of operation depend not only on the general epidemiological situation in a given country, but also on strict co-operation between the surgeon and bacteriologists and pathologists. Results of studies of the drug resistance and biology of the tubercle

TABLE V.—LATE RESULTS PER CENT. RESECTION, THORACOPLASTY, EXTRAPLEURAL PNEUMOTHORAX

Kind of operation (number of cases)	*Sputum negative*	*Sputum positive*	*Mortality*	*Remark*	*Total*	*Working*	*Observation period*
Resection (555)	80·5 95·2*	4·2	4·1	Loss of contact 11·2	100	90·5	1½-8
Thoracoplasty (390)	72·2	6·2	4·8	Sputum (K) condition satisfactory 16·8	100	86·7	1½-12
Extrapleural pneumothorax (574)	76·8 97·8†	8·9	3·3	11·0	100	90·9	1-10

Remark: * that of survivors.
† satisfactory result.

bacilli recovered from sputum and resected lesions form the basis for prognosis, the conduct of further treatment, and the selection of the type, extent, and time of operation.

The most important factor affecting the results is adequate pre-operative chemotherapy. Errors committed by the patient as well as the physician are responsible for the development of resistance to the major drugs. The emergence of drug resistance should always lead to the consideration of surgery.

The results of resection in patients with drug resistant bacilli, when compared with those in patients with sensitive bacilli, are much worse, both in mortality and morbidity. In some countries, for instance Holland, because of well-planned use of antimicrobial drugs based on modern principles, it has been possible to avoid drug resistance in patients under sanatorium care. Under such circumstances surgeons may consider drug resistance a contra-indication to operation. This attitude is similar to that of the surgeon who refuses to operate on a patient with diffuse peritonitis in acute appendicitis after perforation.

Resistance to the major drugs is an indication for surgery, since the outlook for these patients is very poor unless they are operated upon. The solution to this problem lies in the prevention of drug resistance, and not in the treatment of complications, which are avoidable.

In Holland, where surgeons are inclined not to operate on patients with streptomycin resistant bacilli, bronchial fistula is a rare complication. Mètras (1956) in Marseilles reported 500 resections without a single bronchial fistula. Some authors (Nuboer, 1956) claim not to have had any cases complicated by bronchial fistula in recent years. There is a lack of fixed criteria for recognising bronchial fistula. Some authors include only fistulas through large bronchi among the post-operative complications, and not those in smaller bronchi.

Table VI shows the results of resection in a number of published series.

TABLE VI.—PRIMARY MORTALITY IN LUNG RESECTIONS
(After Eerland, modified)

Author	*Year*	*Number cases*	*Per cent.*
Bailey (without SM)	1949	100	27·0
Bailey (with SM)	1949	100	16·0
Clagett	1951	29	3·4
Sellors	1952	286	7·0
P. Thomas	1951	82	7·3
Santy *et al.*	1949	360	5·0
Overholt	1950-52	437	8·9
Edwards *et al.*	1952	729	1·92
Denk	1952	40	12·5
Nuboer	1946-52	371	3·2
Gale	1952	500	4·6
Sweet	1939-45		14·3
Himmelstein	1946-48		9·8
Day	1945-49		6·9
Chamberlain	1946-50		4·0
Johansson	1945-50		13·0
Eerland	1943-59	1,316	2·0
Barret *et al.*	1958	1,567	2·9
U.S.A. (Walkup)	1958	1,958	2·0
Amosow	1959	1,510	2·8
W. Rzepecki	1948-59	1,341	3·6
T. i W. Rzepecki	1951-55	243*	2·5

* Children and adolescents.

TABLE VII.—EARLY MORTALITY
First column = number of operations (in brackets) and their percentages.

Operation	*Mortality*							
	Operative 24 hours		*Institutional to four months*		*Early to 2 months*			
Pneumonectomy ..	5·1 (185)	17·0	16·4 (220)	8·6	19·9 (212)	12·7	5·3 (330)	12·0
Lobectomy	35·1 (1,285)	3·3	41·0 (551)	3·0	55·3 (590)	5·7	38·0 (2,362)	2·7
Segmentectomy ..	42·3 (1,554)	1·0	39·2 (526)	1·9	24·8	0·4	44·0 (2,750)	0·9
Subsegmentectomy ..	17·5 (633)	0·0	3·3 (44)	0·0		(264)	12·7 (794)	0·0
Total	100·0 (3,657)	2·4 (90)	100·0 (1,341)	3·4 (46)	100·0 (1,066)	5·8 (62)	100·0 (6,236)	2·0 (132)
	Steele U.S.A. 1952-55*		Rzepecki Poland 1948-59		Procházka C.S.R. 1949-56†		Walkup U.S.A. 1952-57‡	

* Forty-one institutions.
† Done by sixteen surgeons.
‡ Done by many surgeons in U.S.A.

Edwards and others (1952) report a very low mortality rate of 1·9 per cent. which is one of the lowest in the world literature.

The mortality rate in the series under consideration was 3·4 per cent. which is in the same order as many of the other published ones.

Table VII shows results of the figures of the various forms of resection at this clinic and at others in other parts of the world. In each the mortality falls as the extent of the operation lessens, but again, the results in the series under consideration are similar to the others, and that for pneumonectomy is satisfactory in view of the severity of this disease under treatment.

As in other series, the most important complication has been the development of a bronchopleural fistula. Table VIII gives the incidence of this as reported in a number of papers.

TABLE VIII.—BRONCHIAL FISTULA

Author	*Country*	*Year*	*Number of cases*	*Per cent.*
O'Brien	U.S.A.	1950	202	12·0
Monod	France	1951	112	20·0
Berard	France	1951	230	12·0
Dawidson	U.S.A.	1954	512	16·0
Eerland	Netherlands	1955	1,026	2·0
Mètras	France	1956	493	0·0
Nuboer	Netherlands	1956	1,236	2·6
Procházka	C.S.R.	1956	1,066	12·8
Walkup	U.S.A.	1958	6,290	4·1
Amosow	U.S.S.R.	1955	700	5·1
Amosow	U.S.S.R.	1957-58		7·1
Barret *et al.* ..	U.S.A.	1958	1,567	6·2
W. Rzepecki ..	Poland	1959	1,341	7·2*

* In 1957 = 2·7 per cent.

By 1957 the incidence of fistula in our clinic had fallen to 2·7 per cent., but since then it has risen to 10·3 per cent. because of the rise in the number of patients with drug resistant organisms. There is a close relationship between the findings of active tuberculosis at the site of bronchial section, and fistula (Fig. 6). Harazda (1960) in a study of 721 sections of bronchi found that the highest incidence of fistulæ was found in those cases where active tuberculous granulation tissue was found at the level of transection, and this finding was borne out in this series.

Summary

The operative and post-operative complications in 1,341 operations for pulmonary tuberculosis are discussed.

Bronchial fistula occupies first place among the causes of death, followed by shock, pulmonary embolism, cardio-respiratory failure and specific exacer-

bation. The early mortality within four months in the hospital was 3·6 per cent. (8·6 per cent. in pneumonectomies).

The complications are discussed in detail; the incidence of bronchial fistula decreased from 7·2 per cent. to 2·9 per cent. (1960). Streptomycin resistance and the presence of tuberculous lesions in the bronchus at the site of its section are the most important causes of bronchial fistula.

At present, one out of four patients operated upon has streptomycin resistant bacilli.

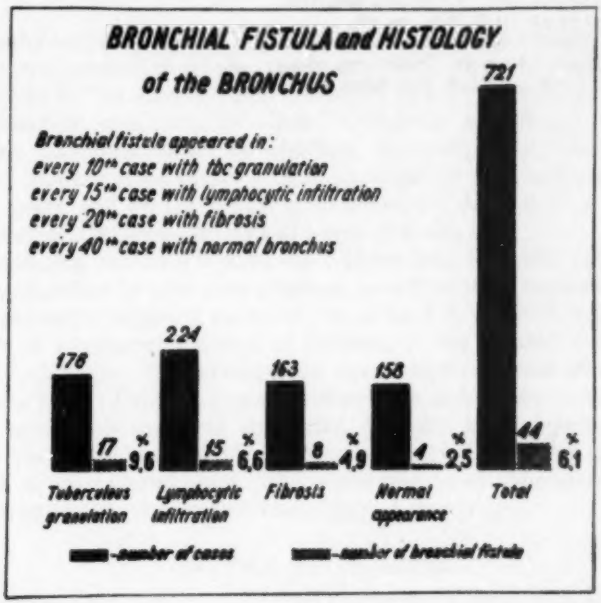

FIG. 6.

The cultural viability of tubercle bacilli recovered from operative specimens, found in 57 per cent. of cases, is due to inadequate previous chemotherapy. The viability of the bacilli in lesions is considered to be the principal cause of complications.

The results of forty-two bilateral one- or two-stage resections are reviewed, with an overall mortality of 7 per cent.: only one patient (2·3 per cent.) now has a positive sputum.

The late comparative results of resection and thoracoplasty and extrapleural pneumothorax are mentioned.

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QUANTITATIVE INVESTIGATIONS OF THE FORCED VITAL SPIROGRAM IN HEALTHY CHILDREN

I. NORMAL VALUES

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The Forced Expiratory Volume (F.E.V.) and Forced Vital Capacity (F.V.C.) test is now widely used in adults, and is one of the most practical and helpful tests available for the assessment of ventilatory function. Although the test has been extensively evaluated in adults (Gandevia and Hugh-Jones, 1957), little work has been done in children. Kennedy *et al.* (1957) published "normal" values for the EFR[40] ($F.E.V._{.0\cdot75} \times 40$) for boys between the ages of 8 and 14 years, and Strang (1959) gave values for the $F.E.V._{.1\cdot0}$ and F.V.C. for boys and girls between the ages of 7 and 18 years.

By measuring the EFR[40] Thursby-Pelham and Kennedy (1958) assessed ventilatory function in asthmatic children as well as their response to steroids.

In an attempt to evaluate the suitability of the F.E.V. and F.V.C. test for the assessment of ventilatory function in children, it was applied to a number of "normal" children. The investigation was carried out from November 1957 to February 1958. This is a report on that work and on the establishment, in children aged 7-16 years, of prediction formulæ for "expected normal" values for the $F.E.V._{.0\cdot75}$, F.V.C., $F.I.V._{.0\cdot75}$ and F.I.V.C. which can be calculated from anthropometric data. The terminology and abbreviations used are those recommended by Gandevia and Hugh-Jones (1957).

Method and Apparatus

Two methods are available for the measurement of the F.V.C. and $F.E.V._{.0\cdot75}$ values.

(1) Gaensler (1951) described a method using an ordinary spirometer with an attachment which accurately recorded on a dial both the total F.V.C. and any volume expired during a pre-set interval.

(2) Tiffneau (1949) and later Kennedy (1953) recorded the spirographic tracing of the F.V.C. on a fast moving kymograph. This is termed the Forced Expiratory Spirogram (F.E.S.). A similar tracing of the Forced Inspiratory Vital Capacity F.I.V.C. is termed the Forced Inspiratory Spirogram (F.I.S.). Details of the form of the F.V.C. and F.I.V.C. are recorded graphically and the volume expired in any desired time interval can be calculated from a single performance. The spirograms provide a permanent record which can be filed and compared quantitatively and qualitatively with later tracings.

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A spirometer similar to that described by Bernstein *et al.* (1952) was used in the present investigation. This has considerable advantages (Bernstein, 1954; Arnott, 1956) over the Benedict-Roth type of apparatus. Because of the expected wide range of volumes in subjects for study, where ages were from 7 to 16 years, two or more spirometers of different capacities would have been ideal, but the aim was to establish a simple and effective test for the clinician. A spirometer which could be used for both adults and children was used although this involved the possibility of some error in the measurement of small volumes.

Experiments with various face-masks and mouthpieces showed that a modified anæsthetic mask of suitable size and shape gave the best results. It had the advantage that the child himself could apply it to his face and secure an airtight fit easily. Nose-clips and mouthpieces were found either to irritate or to amuse some of the children, so that it was difficult to obtain their full concentration and co-operation.

A Super Ten Electric Recording Drum (Palmer's) with a cylinder 12 inches high and 12 inches in diameter was used. The fastest drum speed of 1·67 cm./sec. was employed in every test throughout the investigation. Superfine smooth white glazed paper was used in all recordings.

Material

One hundred and thirty-three "normal" boys and 58 "normal" girls were studied at the Bristol Central Health Clinic. Children belonged to all sections of the community, from varying social classes and schools who attended the clinic for routine examinations and treatment. A full clinical examination was carried out and anthropometric measurements were made in all children, and the criteria on which the child was accepted as "normal" for the investigation were:

(1) A healthy active child, taking part in all normal school activities.
(2) No history of any disease of the respiratory or cardiovascular systems, apart from minor coughs and colds.
(3) No history suggestive of hay fever, eczema, asthma or wheezing.
(4) No abnormal physical signs in the respiratory or cardiovascular systems.

The following physical data were recorded:

(i) The child's age (to the nearest 3 months).
(ii) The standing height (to the nearest $\frac{1}{4}$ inch).
(iii) The sitting height (to the nearest $\frac{1}{4}$ inch).
(iv) Weight (to the nearest pound).

These measurements were made after removal of the child's shoes, with the boys stripped to the waist and the girls divested of all heavy outer clothing. A correction was made for the remaining garments in girls to make the weights for boys and girls comparable. In the measurement of the standing height the routine advised by Krogman (1948) and Sutcliffe and Canham (1950) was followed, and for sitting height the child sat against the measuring stick on a

box 12 inches high. At each measurement the same routine as for measurement of the standing height was then followed.

Method of Conducting Test

The children were examined and the test was carried out whenever it was convenient, and therefore not under basal conditions. The apparatus was shown and demonstrated to the child, the following points being stressed:

(i) He must breathe in as deeply as possible through his open mouth.
(ii) He must then apply the mask firmly to his face, if necessary with the help of the observer.
(iii) He must then blow out through his open mouth as fast and far as possible. (The experience of the observer was of some importance here in judging whether the child had in fact blown a maximum forced expiration.)

All recordings were made in the standing position, with the child stripped of all heavy outer clothing. The drum was set in motion a few seconds before recording any test. Throughout the performance of the test the observer encouraged the child to blow " fast," the emphasis being to " see how steep you can make the curve " rather than on " how far you can blow it." Once the maximum volume had been expelled, as judged from the tracing, the child was asked to breathe in as deeply and as quickly as possible, the emphasis being put again on the speed of inspiration. The following potential sources of error had to be excluded by the operator. The child sometimes started to blow before the mask was firmly applied to his face, or he sometimes pursed his lips instead of blowing through the widely open mouth.

Four to six tracings were recorded for each child, an interval of 2-3 minutes being allowed between each. Conditions of testing did not vary very much and the gas volumes were measured at ambient pressure in a room the temperature range of which was 19°-20°C. Gas volumes were not adjusted to body temperature, ambient pressure conditions, and saturation with water vapour at 37°C. (B.T.P.S.), following the procedure of other workers (Whitfield *et al.*, 1950; Needham *et al.*, 1954; Gandevia *et al.*, 1957). All 122 boys and 55 girls were able to perform the expiratory part of the test satisfactorily, but 2 of the younger boys and 4 of the younger girls were unable to carry out the inspiratory part successfully. All the younger children had some difficulty in carrying out this part of the test. However, rather than confuse and upset them, and so impair their expiratory curves, no additional attempts were made to obtain a better inspiratory curve.

Method of Measuring Spirograms

The Forced Expiratory (F.E.S.) and Forced Inspiratory Spirograms (F.I.S.) were measured with a transparent scale, graduated horizontally in 0·05 litre (50 ml.) vertically in 0·25 second. In most of the spirograms the beginning of expiration was sharply defined, and in these a vertical line was projected

from this point and the zero point of the time and litre scale placed on it with the vertical zero line on the vertical line just mentioned. The total volume and the volume expired in any particular time could then be read directly off the scale. In those spirograms where the start of expiration was not so sharply defined, the steepest part of the curve was projected backwards and the zero point was taken as the intersection of this line with the horizontal as suggested by D'Silva and Kazantzis (1954). A standard time interval of 0·75 second over which to measure the F.E.V. seemed most appropriate in children. The reason for deciding to use this interval was that in all the spirograms both the $F.E.V._{\cdot 0\cdot 75 \text{ second}}$ and $F.E.V._{\cdot 1 \text{ second}}$ were measured. In 10 of the younger children the F.V.C. was expired in under 1 second and in further cases the $F.E.V._{\cdot 1 \text{ second}}$ approached the F.V.C. level.

In each child the spirogram with the highest $F.E.V._{\cdot 0\cdot 75}$ was then taken as representing the best effort. The measurements taken from these expiratory and inspiratory vital spirograms were then recorded as the " normal " values for that particular child.

Results

The time taken for the completion of the F.E.S. and F.I.S. were measured and the average values are given in Table I.

Table I

	F.E.S.	*F.I.S.*
Under 9 years	1·5 sec. (0·6-2·6 sec.)	0·95 sec. (0·6-1·7 sec.)
9-12 years	1·7 sec. (1·1-2·7 sec.)	0·9 sec. (0·6-1·4 sec.)
Over 12 years	1·9 sec. (1·1-2·6 sec.)	1·0 sec. (0·8-1·2 sec.)

Anthropometric and Spirometric Measurements

The $F.E.V._{\cdot 0\cdot 75}$ and F.V.C. were measured in 122 boys and 55 girls and the $F.I.V._{\cdot 0\cdot 75}$ and F.I.V.C. in 120 boys and 51 girls. From these figures the F.E.V. per cent. and F.I.V. per cent. were calculated. (The F.E.V. per cent. and F.I.V. per cent. indicate the $F.E.V._{\cdot 0\cdot 75}$ and $F.I.V._{\cdot 0\cdot 75}$ expressed as a percentage of the F.V.C. and F.I.V.C. respectively.)

Prediction Formulæ

The spirometric ($F.E.V._{\cdot 0\cdot 75}$, F.V.C., $F.I.V._{\cdot 0\cdot 75}$ and F.I.V.C.), and the anthropometric data (age, standing height, sitting height and weight), were statistically analysed by Regression and Correlation Analysis. In the first instance regression lines for expiratory and inspiratory volumes as a function of a single anthropometric characteristic were calculated and subsequently multiple regression lines were fitted, *i.e.* the expiratory or inspiratory volumes were considered as a function of the multiple variables, age, standing height, sitting height and weight. Correlation coefficients (r) were calculated and the

standard deviation of the points around the regression line was determined by calculating the standard error of estimate (σ_z). The methods of calculations used in the analyses of data are the standard ones given in statistical texts (Kendall; Weatherburn).

The results given in the statistical table (Table II) show that all the anthropometric indices are positively correlated with the spirometric measurements, *i.e.* increase with growth, and the degree of correlation is high. The positive correlation between age and the spirometric measurements differs from the negative correlation in adults, *i.e.* with increasing age these figures fall (Hutchinson, 1846; Baldwin *et al.*, 1948).

Because of this high correlation between all four anthropometric measurements and the spirometric values, any one or more, or all four in combination, may be used for the prediction of normal expected values.

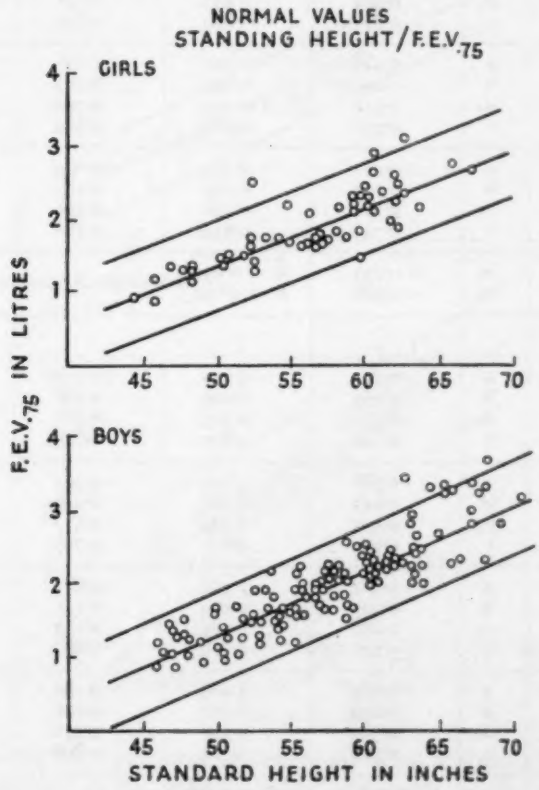

FIG. 1.

APPENDIX

TABLE II.—STATISTICAL TABLE

GIRLS		*Age*	*Standing height*	*Sitting height*	*Weight*
$F.E.V._{.0.75}$ (55 subjects)	a	+0·240	−2·470	−2·702	+0·531
	b	0·145	0·077	0·152	0·016
	σ_z	0·361	0·308	0·316	0·297
	r	0·726	0·809	0·797	0·822
F.V.C. (55 subjects)	a	+0·154	−3·219	−3·438	+0·584
	b	0·186	0·097	0·189	0·020
	σ_z	0·404	0·345	0·341	0·352
	r	0·771	0·839	0·843	0·837
$F.I.V._{.0.75}$ (51 subjects)	a	+0·423	−1·531	−1·656	+0·673
	b	0·093	0·053	0·104	0·010
	σ_z	0·412	0·375	0·372	0·395
	r	0·452	0·582	0·590	0·516
F.I.V.C.	a	+0·211	−3·194	−3·025	+0·721
	b	0·174	0·095	0·173	0·017
	σ_z	0·417	0·348	0·381	0·397
	r	0·710	0·810	0·766	0·742
$F.E.V._{.0.75}$	σ_z	= 0·233	R = 0·895 } Multiple Regression Equation		
F.V.C.	σ_z	= 0·286	R = 0·892 }		
BOYS					
$F.E.V._{.0.75}$ (122 subjects)	a	−0·01	−3·140	−3·706	+0·183
	b	0·165	0·089	0·188	0·021
	σ_z	0·450	0·325	0·365	0·334
	r	0·708	0·860	0·819	0·852
F.V.C. (122 subjects)	a	−0·386	−4·770	−4·937	+0·060
	b	0·247	0·128	0·249	0·031
	σ_z	0·592	0·439	0·577	0·387
	r	0·752	0·873	0·767	0·902
$F.I.V._{.0.75}$ (120 subjects)	a	−0·061	−2·450	−2·874	+0·291
	b	0·133	0·069	0·146	0·016
	σ_z	0·458	0·374	0·257	0·420
	r	0·620	0·719	0·688	0·695
F.I.V.C. (51 subjects)	a	−0·384	−3·885	−6·186	0·190
	b	0·239	0·111	0·286	0·031
	σ_z	0·555	0·526	0·376	0·262
	r	0·761	0·789	0·898	0·952
$F.E.V._{.0.75}$	σ_z	= 0·192	R = 0·881 } Multiple Regression Equation		
F.V.C.	σ_z	= 0·328	R = 0·914 }		

The basic prediction formula is:

Spirometric volume in litres = $a + (b \times \text{Anthropometric measurement}) \pm 2\sigma_z$

This gives the most probable spirometric value, viz. $a + (b \times$ anthropometric measurement), and the bounds about "this most probable" value, within which 95 per cent. of all normal cases should lie.

Thus the relationships between the standing height and the $F.E.V._{\cdot 75}$ and the F.V.C. respectively for girls and boys are given in Figs. 1 and 2. The lines represent the regression line and the bounds within which 95 per cent. of all normal cases should lie.

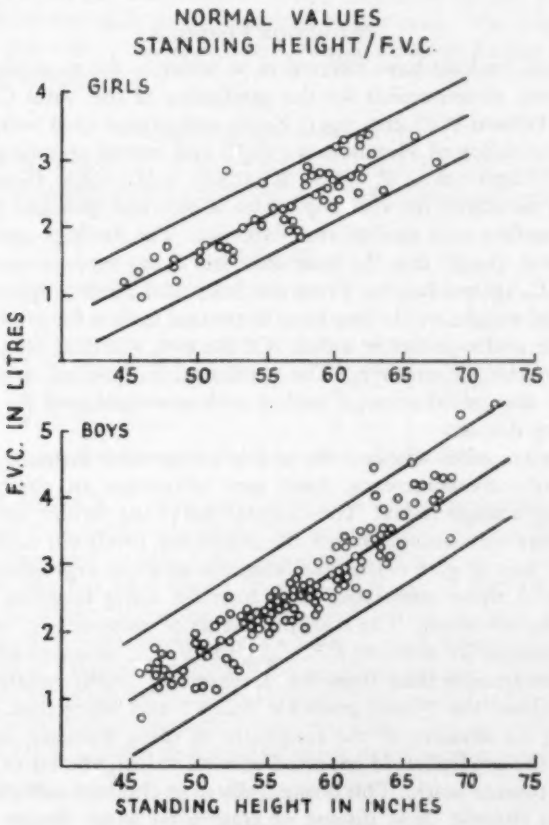

FIG. 2.

The values for "a" represent the intercept on the Y axis by the regression line and a constant in the equation; "b" regression coefficient; "σ_z" the error of estimate for the spirometric measurements and the anthropometric measurements. They are given for boys and girls in Table II.

Multiple Regression Equations for the $F.E.V._{\cdot 75}$ and the F.V.C. and their

dependence upon age, standing height, sitting height and weight were calculated for boys and girls independently using standard statistical methods. The multiple regression formulæ are:

GIRLS:

$$\text{F.E.V.}_{\cdot 0\cdot 75} \text{ in litres} = 1\cdot 2875 + 0\cdot 0098X_1 + 0\cdot 0357X_2 + 0\cdot 0106X_3 + 0\cdot 00855X_4 \quad (\sigma_z = 0\cdot 233)$$

$$\text{F.V.C. in litres} = -2\cdot 2379 + 0\cdot 0232X_1 + 0\cdot 0404X_2 + 0\cdot 0441X_3 + 0\cdot 0074X_4 \quad (\sigma_z = 0\cdot 286)$$

BOYS:

$$\text{F.E.V.}_{\cdot 0\cdot 75} \text{ in litres} = -2\cdot 4080 + 0\cdot 0044X_1 + 0\cdot 0371X_2 + 0\cdot 0504X_3 + 0\cdot 0079X_4 \quad (\sigma_z = 0\cdot 192)$$

$$\text{F.V.C. in litres} = -0\cdot 9118 + 0\cdot 0413X_1 + 0\cdot 0396X_2 - 0\cdot 0413X_3 + 0\cdot 0231X_4 \quad (\sigma_z = 0\cdot 328)$$

X_1 = age, X_2 = standing height, X_3 = sitting height, X_4 = weight.

PREDICTION FORMULÆ

In the past, authors have differed as to which is the most important single anthropometric measurement for the prediction of the Vital Capacity; some (Moore and Gibson-Williams, 1951; Ferris *et al.*, 1952) used body surface area, whereas others followed Hutchinson (1846) and regard standing height as the main index (Engstrom *et al.*, 1956; Kennedy *et al.*, 1957; Hennieson, 1958). Jones (1955) measured the vital capacities of boys and girls and plotted height, weight and surface area against vital capacity. The findings agreed with those of Baldwin *et al.* (1948) that the most smoothly rising curve in each sex was that recording V.C. against height. From the Statistical Table it appears that standing height and weight are the two most important indices for prediction formulæ using a single anthropometric index. Of the two, standing height is probably the more important in children. The prediction of expected normal values for sick children may be fallacious if indices such as weight used for the prediction are altered by disease.

The question arises whether the multiple regression formulæ, using all four anthropometric measurements, have any advantage in clinical work over formulæ using a single index. The calculations in the former are more complicated and time consuming. When the results for predicted normal values for a " normal " boy or girl, calculated from the multiple regression formulæ, are compared with those calculated from formulæ using standing height alone, the differences are small. The standard errors of estimate (σ_z) for the multiple regression equation for both the $\text{F.E.V.}_{\cdot 0\cdot 75}$ and F.V.C. in boys and girls (Statistical Table) are smaller than those for the standing height equation, narrowing the bounds about the " most probable value " and being thus an advantage. Nevertheless, on account of the simplicity of using standing height alone as an index in the prediction of expected normal values, the latter is the method of choice for routine work. This is especially so in children suffering from conditions such as chronic chest disease or congenital heart disease where weight may be altered to a larger extent than standing height by the disease (Heese: results to be published).

F.E.V. PER CENT. AND F.I.V. PER CENT.

No statistical analyses were carried out on the calculated F.E.V. per cent. and F.I.V. per cent. values, but these values were plotted against age and

standing height. From inspection of the scatter diagrams and by using the graphical procedure of drawing freehand a line through the scatter of points, a linear trend showing a fall in the F.E.V. per cent. with an increase of age or standing height could be deduced in the case of boys. No similar trend is obvious in girls. The F.E.V. per cent. in boys varies from approximately 85 per cent. in the 7-year-old to approximately 70 per cent. in the 16-year-old. The scatter of points around this line is large and the lower limits in normal boys are estimated at approximately 60-65 per cent. depending on age. In girls the F.E.V. per cent. are higher, reflecting their smaller F.V.C. values. The average value for the F.E.V. per cent. in girls is approximately 80 per cent. with the lower limits in normal girls in the region of 70 per cent. The scatter of points for the F.I.V. per cent. is so large that it excludes it from having any value in ventilatory assessment.

Difference in Sexes

Values for the $F.E.F._{\cdot 0\cdot 75}$, F.V.C., $F.I.V._{\cdot 0\cdot 75}$ and F.I.V.C. calculated for a girl and boy of standing height 57 inches from the prediction formulæ are given in Table III.

Table III

	Girl	*Boy*
$F.E.V._{\cdot 0\cdot 75}$ in litres	1·919	1·933
F.V.C. in litres	2·310	2·526
$F.I.V._{\cdot 0\cdot 75}$ in litres	1·490	1·483
F.I.V.C. in litres	2·221	2·442

A tendency for the V.C. to be smaller in girls has been recorded, but on the whole V.C. values in boys and girls of the same height are very similar (Ferris *et al.*, 1952; Ferris and Smith, 1953; Jones, 1955; Engstrom *et al.*, 1956). No similar comparison has been made for the $F.E.V._{\cdot 0\cdot 75}$, F.V.C., $F.I.V._{\cdot 0\cdot 75}$ and F.I.V.C. In the present series the F.V.C. and F.I.V.C. are 11·3 per cent. and 9·9 per cent. larger respectively in boys than in girls, when these values are calculated from prediction formulæ using standing height. This difference is large enough to be of practical clinical importance and it justifies the employment of separate prediction formulæ for the two sexes. The sex differences in the $F.E.V._{\cdot 0\cdot 75}$ and $F.I.V._{\cdot 0\cdot 75}$ can be regarded as too small to be of practical clinical importance.

Interrelation of Anthropometric and Spirometric Measurements

Of the anthropometric measurements the standing height, sitting height and weight all show close correlation with the $F.E.V._{\cdot 0\cdot 75}$ and the F.V.C. values in boys and girls, and also with the F.I.V.C. in boys and to a lesser extent in girls. Age shows less correlation with these spirometric measurements. The correlation between the $F.I.V._{\cdot 0\cdot 75}$ and the anthropometric measurements is

much lower (Table II), in agreement with similar findings by Kennedy *et al.* (1957). They also found the correlation coefficients between the IFR[40] and anthropometric measurements to be lower than that for the EFR[40].

Because of the lower correlation coefficients between the $F.I.V._{0\cdot75}$ and F.I.V.S. and the anthropometric measurements, and the difficulty some children had in performing a satisfactory F.I.S., the $F.E.V._{0\cdot75}$ and F.V.C. must be regarded as more suitable for the evaluation of ventilatory function in children.

Comparison of Spirometric Values with other Series

The F.V.C. The values for the F.V.C. in the present series differ from those of Strang (1959) in that the volumes were not corrected to B.T.P.S. and the test was performed in the standing position. In Table IV Strang's F.V.C. values and those of the present series for a child with a standing height of 55 inches are compared with the values for the V.C. in recent publications. According to Ferris and Smith (1953) corrections to B.T.P.S. on the average increase the volumes by 7-9 per cent. Correction of the values for the F.V.C. to B.T.P.S. in the present series results in volumes lower than Strang's but higher than the V.C. values given in Table IV. These higher values for the F.V.C. compared with those for the V.C. might well be a reflection of the employment of the Bernstein-type of spirometer in the former series.

The $F.E.V._{0\cdot75}$. The only other comparable series for $F.E.V._{0\cdot75}$ values has been published by Kennedy *et al.* (1957). Using their prediction formula and calculating the $F.E.V._{0\cdot75}$ for a boy aged 12 years with a standing height of

Table IV.—Comparison of F.V.C. and V.C.

Author	*Predicted value in litres*	*S.D.*	*Spirometer*	*Values corrected to B.T.P.S.*
55 girls	F.V.C. = 2·116	0·345	Bernstein type	No
Present Series				
122 boys	F.V.C. = 2·270	0·439	Child standing	
209 girls	F.V.C. = ±2·40	0·20	Bernstein type	Yes
Strang (1959)				
209 boys	F.V.C. = 2·56	0·33	Child sitting	
Ferris and Smith (1953): 233 girls	V.C. = 2·190	0·27	Benedict-Roth type	Yes
Ferris *et al.* (1952): 161 boys	V.C. = 2·270	0·45	Child standing	
Kennedy *et al.* (1957): 175 boys	V.C. = 2·028	0·290	Gilson and Hugh-Jones. Child sitting	Yes
Engstrom *et al.* (1956): 50 boys, 43 girls	V.C. = 2·276	±12·6%	Benedict-Roth type. Child sitting	Yes

57 inches a value of 1·950 litres (±0·268) is obtained. Using the multiple regression formula for a boy of similar age and height, sitting height of 30·25 inches and weighing 86 lb. (approximate average values for a boy in the present series), a value of 1·964 litres (±0·192) is obtained. Although the mean of four readings for their EFR[40] values were taken and values corrected to 37°C. and saturated with water vapour, the similarity of the predictions in the two series using different apparatus and technique suggest that these $F.E.V._{0·75}$ values could probably be accepted as standard normal. The plea by D'Silva and Kazantzis (1954) that each laboratory should determine its own values for "normal" falls away if Kennedy's and the present series' values for the $F.E.V._{0·75}$ are both accepted as standard normal.

F.I.V.$_{0·75}$. The only other comparable series for the $F.I.V._{0·75}$ in children is again that of Kennedy *et al.* (1957). Calculations for a boy with a standing height of 55 inches according to their formula gives a value for the $F.I.V._{0·75}$ of 1·773 (±0·393) litre. The value is considerably higher than the value of 1·345 (±0·374) for a corresponding child in the present series. The discrepancy is not surprising and the difficulty of obtaining an adequate F.I.S. in the present series has already been discussed.

F.I.V.C. No literature on the F.I.V.C. in children is available for purposes of comparison.

Summary

1. Anthropometric and spirometric investigations were carried out on 122 "normal" boys and 55 "normal" girls. The spirometric recordings consisted of Forced Expiratory and Forced Inspiratory Spirograms. Their characteristics were investigated.

2. The $F.E.V._{0·75}$ and F.V.C. were measured from the Forced Expiratory Spirograms in 122 boys and 55 girls; the $F.I.V._{0·75}$ and F.I.V.C., in 120 boys and 51 girls.

3. The corresponding F.E.V. per cent. and F.I.V. per cent. values were calculated for each child.

4. The values obtained for the $F.E.V._{0·75}$, F.V.C., $F.I.V._{0·75}$ and F.I.V.C. were statistically analysed.

5. Prediction formulæ using a single anthropometric index and multiple regression formulæ using age, standing height, sitting height and weight were calculated for boys and girls independently. The prediction formulæ using standing height alone, as an index in the prediction of "expected normal" spirometric values, is considered to be the method of choice for routine work.

6. The $F.E.V._{0·75}$, F.V.C. and F.E.V. per cent. are more suitable values for the evaluation of ventilatory function in children than the $F.I.V._{0·75}$, F.I.V.C. and F.I.V. per cent.

7. The Forced Expiratory Volume and Forced Vital Capacity Test has been found to be suitable for the assessment of ventilatory function in children over the age of 7 years. It is a simple, interesting, easily performed and repeatable test.

It is with pleasure that I record my thanks to Professor A. V. Neale who supplied the stimulus and inspiration for this piece of work, and to Dr. Smallwood who made available facilities at the Central Health Clinic; Sister Miller was of much help here.

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QUANTITATIVE INVESTIGATIONS OF THE FORCED VITAL SPIROGRAM IN HEALTHY CHILDREN

II. THE EFFECT OF:

(i) REPEATED TESTING AT VARYING INTERVALS
(ii) POSTURE
(iii) ISOPRENALINE INHALATION

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The Forced Expiratory Volume and Forced Vital Capacity Test has been found to be suitable for the assessment of ventilatory function in children over the age of 7 years (Kennedy *et al.*, 1957; Engstrom *et al.*, 1956; Strang, 1959; Heese, 1961). It is a simple, interesting and easily performed test and is most suitable for the assessment of ventilatory function in children suffering from asthma (Thursby-Pelham and Kennedy, 1958; Heese, to be published).

The effects of factors such as learning, day-to-day variation and change of posture have not been investigated previously. Changes in weather conditions in general have no statistically significant effect on the $F.E.V._{0\cdot75}$ and F.V.C. values in normal children (Heese, unpublished results).

Improvement in the measured values for the F.E.V. and F.V.C. in response to a bronchodilator drug, given orally, by inhalation or injection, is widely used to indicate the presence of reversible bronchospasm (Rossier, 1949; Snider *et al.*, 1955; Kennedy and Thursby-Pelham, 1956; Hume and Gandevia, 1957; Gandevia *et al.*, 1957). Before attempting to assess the bronchodilator effect of drugs in asthma, it remains to show how normal children respond to them on spirometry. This paper is a report on that aspect of the subject. The corresponding report on asthmatic children will be published in due course.

Material and Method

These factors were studied in " normal " children seen at the Central Health Clinic (Heese, 1961) in the Out-patient Department or wards of the Royal Hospital for Sick Children, Bristol. None of the " hospital " cases gave a history or showed clinical or radiological evidence of past or present chest disease. The technique used for taking anthropometric and spirometric measurements was the same as in a previous study (Heese, 1961). The recorded $F.E.V._{0\cdot75}$ and F.V.C. values were those measured from the spirogram showing the highest $F.E.V._{0\cdot75}$ and F.V.C. values of the 4-6 tracings taken on a particular occasion. The values obtained for the " hospital " cases were all well within

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the normal range and it seems reasonable to assume that they were actually, and not merely nominally, normal subjects in a respiratory sense.

(*a*) *Repeated Testing at Varying Intervals*

The effect of learning, that is, whether any significant improvement occurred in the F.E.V.$_{0\cdot75}$ and F.V.C. values on repetition of the test (*a*) after an interval of 30 minutes and (*b*) after a number of days, was studied. This last investigation also provided the opportunity of studying the normal day-to-day variations in these values. In (*a*) the test was carried out as described and repeated after an interval of 30 minutes in 21 boys and 4 girls. In (*b*) the test was carried out repeatedly, over a period of days, in 28 boys and 6 girls. These tests were always made in the morning at approximately the same time. The test was repeated on a total of 131 occasions (variation 2-9). The variations seen in " normals " and in patients with congenital heart disease cases are small and differ from the large variations seen from day to day in the asthmatic child.

TABLE I.—AVERAGE VALUES AND STANDARD DEVIATIONS OBTAINED FOR F.E.V.$_{0\cdot75}$, F.V.C. AND F.E.V. PER CENT.

		Average F.E.V.$_{0\cdot75}$ in L.	*Average F.V.C. in L.*	*Average F.E.V. per cent.*
(*a*) Repeated testing after 30 minutes	First reading	1·678 S.D. ±0·318	2·105 S.D. ±0·438	80 S.D. ±6·7
	Second reading	1·664 S.D. ±0·358	2·097 S.D. ±0·436	79·4 S.D. ±7·4
(*b*) Learning effect over days	First reading	2·093 S.D. ±0·548	2·592 S.D. ±0·689	81·0 S.D. ±6·2
	Second reading	2·090 S.D. ±0·597	2·571 S.D. ±0·665	81·0 S.D. ±6·9
(*c*) Effect of change of posture	Standing to sitting	1·512 S.D. ±0·383	1·873 S.D. ±0·495	80 S.D. ±7·6
		1·480 S.D. ±0·385	1·853 S.D. ±0·501	80 S.D. ±8·5
	Standing to supine	1·533 S.D. ±0·346	1·923 S.D. ±0·449	80 S.D. ±7·7
		1·410 S.D. ±0·383	1·826 S.D. ±0·452	77 S.D. ±9·1
(*d*) Effect of isoprenaline inhalation	First reading	1·558 S.D. ±0·396	1·914 S.D. ±0·512	81 S.D. ±7·3
	Second reading	1·536 S.D. ±0·405	1·925 S.D. ±0·475	80 S.D. ±7·8

For purposes of statistical analyses the first and last available readings for each child were used. The time interval between these two readings was usually less than two weeks and never more than three weeks.

(*b*) *The Effect of Posture*

The effect on the F.E.V.$_{0\cdot75}$ and F.V.C. values of changing from a standing to a sitting position was studied in 20 children (15 boys and 5 girls). The test was carried out on 43 occasions (variation 1-5) in the usual way in the standing position and then after an interval of 15 minutes repeated in the sitting position.

The effect on the F.E.V.$_{0\cdot75}$ and F.V.C. values of changing from a standing to a supine position was studied in 18 of the same children (14 boys and 4 girls). The test was carried out in the usual way in the standing position and repeated after 15 minutes lying supine without a pillow, giving a total of 35 observations (variations 1-5).

(*c*) *The Effect of Isoprenaline Inhalation*

Twenty normal children (15 boys and 5 girls) were seen on thirty-two occasions (variation 1-4) and the F.E.V.$_{0\cdot75}$ and F.V.C. measured in each child before and after two inhalations of isoprenaline from a Medihaler-Iso (Riker). The interval between the tests was 15 minutes. The recorded F.E.V.$_{0\cdot75}$ and F.V.C. values were those measured from the spirogram showing the highest F.E.V.$_{0\cdot75}$ value of the 4-6 taken on a particular occasion. The volumes by which the post-isoprenaline values differed from the pre-inhalation values were noted and analysed. The increases and decreases after isoprenaline were expressed as percentages of the pre-inhalation values.

Results

The average and standard deviations for the F.E.V.$_{0\cdot75}$, F.V.C. and F.E.V. per cent. recorded in the investigation of effects of the mentioned factors are given in Table I.

(*a*) *Repeated Testing at Varying Intervals*

The volumes by which the F.E.V.$_{0\cdot75}$ and F.V.C. levels differed in (*a*) and (*b*) from the initial readings were recorded as positive and negative values. In (*a*) (*i.e.* after repeating the test following an interval of 30 minutes) these

Table II

Test repeated		*Largest increase*	*Largest decrease*
(*a*) After 30 minutes	F.E.V.$_{0\cdot75}$	225 ml. (11·8%)	275 ml. (17·7%)
	F.V.C.	150 ml. (5·7%)	150 ml. (5·8%)
(*b*) After days	F.E.V.$_{0\cdot75}$	550 ml. (17%)	250 ml. (16%)
	F.V.C.	275 ml. (13·5%)	525 ml. (19·4%)

changes were—with two exceptions for the F.E.V.$_{0\cdot75}$—always within the ± 10 per cent. range. The absolute changes in the volumes were, furthermore, very small and in the range ± 100 ml. for the F.E.V.$_{0\cdot75}$ and F.V.C. in 80 per cent. and 88 per cent. of cases respectively. In (*b*), where the time interval was not minutes but days, the changes were again in the majority of cases (88·2 per cent. and 94·1 per cent. for the F.E.V.$_{0\cdot75}$ and F.V.C. respectively) within the ± 10 per cent. range, although the number of cases with changes in the ± 100 ml. range was much less (64·4 per cent. and 55·9 per cent.) than in (*a*).

The largest increases and decreases recorded for the F.E.V.$_{0\cdot75}$ and F.V.C. in (*a*) and (*b*) are given in Table II.

The changes in the volumes of the F.E.V.$_{0\cdot75}$ and F.V.C. in (*a*) and (*b*) were statistically analysed and t-tests were made. These showed that the differences between the volumes of the two readings for the F.E.V.$_{0\cdot75}$ and F.V.C. in both (*a*) and (*b*) were not significant, and no learning effect is therefore apparent.

(*b*) *The Effect of Change in Posture*

The changes in volume for the F.E.V.$_{0\cdot75}$ and F.V.C. in the sitting and supine positions are compared in Table III.

TABLE III

		Decrease	*Same*	*Increase*
Change from standing to sitting	F.E.V.$_{0\cdot75}$	21 (49%)	12 (28%)	10 (23%)
	F.V.C.	23 (53·5%)	4 (9·5%)	16 (37%)
Change from standing to sitting	F.E.V.$_{0\cdot75}$	30 (86·7%)	—	5 (13·3%)
	F.V.C.	30 (86·7%)	—	5 (13·3%)

In the statistical check on the volume changes t-tests were made. These results are given in Table IV and it is apparent that the postural changes are significant for change of posture from standing to sitting at the 5 per cent. level and standing to supine at the 0·1 per cent. level.

TABLE IV

Change of posture			*Degrees of freedom*	*Critical value at 5% level significance*
Standing to sitting	F.E.V.$_{0\cdot75}$	2·53	42	2·02
	F.V.C.	2·19	42	2·02
Standing to supine	F.E.V.$_{0\cdot75}$	5·362	34	2·03
	F.V.C.	5·625	34	2·03

(*c*) *The Effect of Isoprenaline Inhalation*

All the changes in the $F.E.V._{\cdot 0 \cdot 75}$ values were within the $\pm$ 10 per cent. range of the initial observation, with the exception of 1 child who showed an increase of 11·8 per cent. The F.V.C. changes were also within the $\pm$ 10 per cent. range of the initial observation with one exception which showed a decrease of 12·3 per cent. from this observation. The volumes obtained in the post-isoprenaline $F.E.V._{\cdot 0 \cdot 75}$ were in 10 cases larger than the pre-isoprenaline value; in 4 cases they remained the same, and in 18 cases they were smaller. The post-isoprenaline values for the F.V.C. has increased in 15 cases, remained unchanged in 1 case and decreased in 16 cases.

The results were analysed and t-tests were made and the following results obtained:

	t	*Degrees of freedom*	*Critical value at the 5% level*
$F.E.V._{\cdot 0 \cdot 75}$ ..	2·827	31	2·04
F.V.C. ..	2·008	31	2·04

When statistically analysed, the post-isoprenaline valves obtained for the $F.E.V._{\cdot 0 \cdot 75}$ were found to be significantly lower than the pre-isoprenaline values not only at the 5 per cent. level but also 1 per cent. level ($P = 2 \cdot 75$). No significant change was observed for the F.V.C. values.

Discussion

No appreciable learning effect could be demonstrated on repeating the test (*a*) after 30 minutes and (*b*) over, or after a number of days.

All differences recorded in (*a*) between the $F.E.V._{\cdot 0 \cdot 75}$ and F.V.C. values of the first and second readings (with two exceptions for the $F.E.V._{\cdot 0 \cdot 75}$) were within the $\pm$ 10 per cent. range. The corollary to these findings is that changes in the $F.E.V._{\cdot 0 \cdot 75}$ and F.V.C. values of 10 per cent. or more after, for instance, bronchodilator drugs may fairly be attributed to the effects of the drug. This would be in accordance with findings in adults (Gandevia *et al.*, 1957; Thomson and Hugh-Jones, 1958).

In those cases where the test was carried out repeatedly over a period of days, the day-to-day variations of the $F.E.V._{\cdot 0 \cdot 75}$ and F.V.C. expressed as a percentage of the initial value was also, in the majority of cases, within the $\pm$ 10 per cent. range of the initial value. In all the cases the daily values, regardless of the variations, were within the predicted normal range for the particular child (Heese, 1961). The relatively large variations, however, that may occur in certain normal individuals from day to day must be taken into consideration when the test is being used in the assessment of daily improvement or deterioration in pathological conditions.

The inference from the statistical analysis (Table IV) is that there was a definite decrease in the volume expired when the posture was changed from

standing to sitting. When the average decrease is expressed as a percentage of the average initial volume in the standing position, it is found to be small ($F.E.V._{.0\cdot75} = 2\cdot05$ per cent. and F.V.C. = 1·02 per cent. Table V.) In practical work in normal children, values obtained for the $F.E.V._{.0\cdot75}$ and F.V.C. in the standing and sitting positions can probably be regarded as being comparable. However, this may not be so in sick children and should be investigated.

TABLE V.—EFFECTS OF CHANGE OF POSTURE

	Average standing value	*Average sitting value*	*Average fall per cent.*	*Average standing value*	*Average supine value*	*Average fall per cent.*
$F.E.V._{.0\cdot75}$ ..	1·512	1·480	2·05	1·533	1·410	8·02
F.V.C.	1·873	1·853	1·02	1·923	1·826	5·04

The lowering of the $F.E.V._{.0\cdot75}$ and F.V.C. values by 8·02 per cent. and 5·04 per cent. respectively by changing from the standing to the supine position, when statistically analysed, was significant. The lowering of the F.V.C. is in agreement with the lowering reported in the V.C. by changing from the erect to the supine position (Hutchinson, 1849; Wade and Gilson, 1951; Whitfield *et al.*, 1950; Michelson and Lowell, 1958). Bohr (1907) suggested that a period of 40 minutes or longer was necessary for the alterations in the lungs produced by postural change to become maximal, but Livingstone (1928) and Whitfield *et al.* (1950) suggested that the maximal changes occurred within the space of 2-5 breaths. In the present series 15 minutes was allowed between the takings of the two readings.

The lowering of the $F.E.V._{.0\cdot75}$ with the change from the erect to the supine position is in agreement with the findings of Attinger *et al.* (1956) who studied the mechanics of breathing in the sitting, supine and prone positions. They found that mechanical resistance, including the resistance to airflow, *per se*, and the resistance to tissue deformation was usually highest in the supine position and lowest in the sitting position. Michelson and Lowell (1958), who compared values for the $F.E.V._{.1\ sec.}$ in adults measured in the erect and in the recumbent positions, could demonstrate no significant change.

The statistically significant lowering of the $F.E.V._{.0\cdot75}$ value following the inhalation of isoprenaline was unexpected and the explanation is not readily found. It may have been a psychological effect. These " non-asthmatics " as opposed to asthmatics usually objected to the inhalations and this may have had an upsetting effect on the subsequent performance of the child and on the spirogram. Furthermore, it must be noted that the average lowering of the $F.E.V._{.0\cdot75}$ level was only 1·4 per cent. It seems unlikely that isoprenaline inhalation might have a hitherto unsuspected effect on the normal bronchial tree. The effect of drugs on the pulmonary ventilation of normal children as judged by the $F.E.V._{.0\cdot75}$ and F.V.C. test needs further investigation using a

larger series of cases and a control " blank " inhalation with a scent acceptable to the test subjects.

The response is different from that obtained from asthmatic subjects. The presumed psychological effect in the normal children has been noted and the improvement in asthmatic children from the inhalation of the drug, in spite of any possible psychological upset, must all the more certainly be attributed to the drug itself and not to the ritual employed, the odour, or any other factor.

Conclusions

No learning effect could be demonstrated in the $F.E.V._{0\cdot75}$ and F.V.C. values on repeating the test after 30 minutes or over a period of days.

The $F.E.V._{0\cdot75}$ and F.V.C. values vary from day to day. This variation expressed as a percentage of the initial value is, in the majority of cases, within the $\pm$ 10 per cent. range.

A statistically significant decrease in the $F.E.V._{0\cdot75}$ and F.V.C. values has been shown to occur in changing (*a*) from a standing to a sitting position and (*b*) from a standing to a supine position. The average decrease seen in (*a*) is so small that it can be ignored in practical work. However, the lowering of the $F.E.V._{0\cdot75}$ and F.V.C. values seen in (*b*) warrants consideration when the test is performed in the supine position.

Any increase in the $F.E.V._{0\cdot75}$ and F.V.C. of more than 10 per cent., *i.e.* the upper limit of normal variation, after the inhalation of isoprenaline in children can be regarded as significant and indicative of the beneficial effect of the drug.

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TOBACCO, ALCOHOL AND TUBERCULOSIS

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Opinions differ about the influence of tobacco smoking and alcohol consumption upon tuberculosis. In Britain Lowe (1956) found that tuberculous patients before diagnosis smoked more heavily than controls. He suggested that smoking might predispose to tuberculosis. Alcohol consumption has been suspected as a factor in the ætiology of tuberculosis for many years, but the evidence has been inconclusive (Rich, 1946).

As heavy drinkers are likely to be heavy smokers (Cartwright *et al.*, 1959), an association between either alcohol or tobacco with tuberculosis will lead to the finding that both alcohol and tobacco are consumed in excess by tuberculous patients whether or not both are causally related to tuberculosis. Therefore in re-investigating this relationship it was thought advisable to attempt to assess the relative importance of both factors.

Method and Materials

A simple questionnaire was designed to give information about the smoking and drinking habits of tuberculous patients before diagnosis, and of controls.

The tuberculous group of 102 were consecutive new admissions to the Macleod Repatriation Sanatorium, Victoria, and were otherwise unselected. The majority of all new cases of pulmonary tuberculosis amongst Victorian ex-servicemen are treated at this Sanatorium and the admissions provide a large sample of the total cases diagnosed during the period of investigation.

The control group of 104 were also ex-servicemen who were a random sample of those admitted to the surgical wards of the Repatriation Hospital, Heidelberg. Those in orthopædic wards were excluded because of a possible relationship between accidents and alcohol.

Owing to the broad nature of the Repatriation provisions, cases in the surgical wards represent a cross-section of the ex-servicemen in Victoria. Moreover, as ex-servicemen make up a large proportion of the male population, it is probable that the controls provide a cross-section of the Victorian male population in the age groups investigated. Similarly the tuberculous patients represent a reasonable sample of the older tuberculous male patients in Victoria.

Although participation in the investigation was voluntary the response was almost universal, only two prospective controls, and none of the tuberculous patients refused to co-operate. One of us (K.B.) conducted the investigation at Macleod and ward sisters handled the questionnaires at Heidelberg. The subjects completed the questionnaires unaided. To encourage accurate statements, the replies remained anonymous. The completed unidentified questionnaire was placed in a sealed envelope before being surrendered for

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inspection. In two cases in each group the result was discarded as the information was incomplete. The final number in each group was 100.

An additional investigation was conducted by one of us (A.H.C.) in Queensland where a large group of ex-servicemen with tuberculosis were asked by medical officers to complete a questionnaire about their smoking habits, before and after the diagnosis of tuberculosis. Controls of approximately the same age distribution were obtained from patients in the casualty wards of Brisbane hospitals by three medical students. Anonymity was not sought in this part of the investigation.

The Queensland group consisted of consecutive tuberculous inpatients and a random sample of tuberculous patients attending the Repatriation Outpatient Clinic. Tuberculosis had been diagnosed some years before in the majority of the outpatients. Consequently comparison with the present smoking habits of the controls is only reliable provided these have remained reasonably constant for some years. Low (1956) in a similar investigation found that any difference due to this factor was most unlikely to have influenced the results.

Results

Alcohol Consumption.—For convenience the alcohol consumption has been expressed as the amount of ethyl alcohol consumed. The average alcohol consumption of the tuberculous patients before diagnosis was found to be 73 ml. of ethyl alcohol daily. This is equivalent to nine 7-ounce glasses of beer daily. The controls had a much lower alcohol consumption of 23 ml. of ethyl alcohol daily, which is the equivalent of almost three glasses of beer daily. The difference between the two groups is highly significant ($t = 6{\cdot}65$, $P < 0{\cdot}001$).

The alcohol consumption has been divided into seven grades and the tuberculous group compared with the controls (Table 1). There is a definite de-

Table 1.—Daily Consumption of Alcohol (ml.) of Tuberculous Patients and Controls

	Nil	*10-25*	*26-50*	*51-75*	*76-100*	*101-125*	*126+*	*Total*
Tuberculous group before diagnosis of tuberculosis	11	14	20	21	11	9	14	100
Controls	34	27	26	7	4	1	1	100

$x^2 = 44{\cdot}56$. $P < 0{\cdot}001$.

With the fourth and fifth columns and the sixth and seventh colums amalgamated, $n = 4$.

ficiency of non-drinkers and light drinkers of alcohol amongst the tuberculous group which has an excess of heavy consumers of alcohol. The difference is highly significant ($x^2 = 44{\cdot}56$, $n = 4$, $P < 0{\cdot}001$).

Smoking Habits.—In calculating the smoking habits, 1 ounce tobacco per week has been regarded as the equivalent of four cigarettes daily with the exception of the pipe smokers in Queensland who were classified separately. The number of cigarettes smoked has been classified into six grades and the

TABLE 2.—NUMBER OF PERSONS SMOKING STATED NUMBER OF CIGARETTES DAILY (VICTORIA)

	Nil	*1-9*	*10-19*	*20-29*	*30-39*	*40+*	*Total*
Tuberculous group prior to diagnosis ..	9	9	27	29	13	13	100
Controls	23	5	29	27	12	4	100

With the fifth and sixth columns amalgamated, $n = 4$.

$x^2 = 9{\cdot}48$. $0{\cdot}05 > P > 0{\cdot}02$.

tuberculous group has been compared with the controls (Table 2). There is a significant excess of tobacco consumption amongst the tuberculous group. There is a similar difference between the controls and tuberculous patients in Queensland (Table 3) who were shown also to have reduced their smoking habits after the detection of their tuberculosis.

TABLE 3.—PERCENTAGE OF SAMPLE CONSUMING STATED NUMBER OF CIGARETTES DAILY (QUEENSLAND)

	Nil	*1-9*	*10-19*	*20-29*	*30-39*	*40+*	*Pipe*	*Total*
Prior to diagnosis of tuberculosis	9·1 (28)	10·5 (32)	34·3 (105)	26·8 (82)	7·2 (22)	6·2 (19)	5·9 (18)	100% (306)
Controls	19·9 (44)	15·4 (35)	19·5 (43)	25·8 (57)	5·4 (12)	9·1 (20)	4·6 (10)	100% (221)

Actual numbers in parenthesis.

$x^2 = 41{\cdot}12$. $n = 6$. $P < 0{\cdot}001$.

Relationship between Alcohol and Tobacco Consumption.—It is of some importance to determine whether heavy alcohol and tobacco consumption are more common in the same individuals and to decide whether either or both are linked with an increased incidence of tuberculosis.

When the controls are examined, it is found that those consuming more than 26 ml. of ethyl alcohol daily are more likely to be heavy smokers than those consuming less than 26 ml. daily (Table 4). As the difference is significant, it

TABLE 4.—RELATIONSHIP BETWEEN ALCOHOL AND TOBACCO CONSUMPTION. NON-TUBERCULOUS CONTROLS

	Light smokers 0-9 cigs. daily	*Moderate and heavy smokers*	*Total*
Light drinkers 0-25 ml. daily	24 (39%)	37 (61%)	61 (100%)
Moderate and heavy drinkers 26 ml. or more daily	4 (10%)	35 (90%)	39 (100%)

$x^2 = 8{\cdot}6$. $P < 0{\cdot}01$.

appears that smoking and drinking habits tend to be linked together quite independently of tuberculosis. Consequently only one of the habits need be related to tuberculosis for both to be found excessive in the tuberculous group.

The relationship of alcohol or smoking to tuberculosis can be examined separately after matching the tuberculous patients and controls according to alcohol consumed or tobacco smoked.

When the tuberculous group and controls were matched according to alcohol consumed, it was found that the tuberculous group had a similar distribution of smokers as the controls. There was no significant difference between the two. After some of the smaller groups have been amalgamated then, $n = 6$ and $x^2 = 5{\cdot}94$, $0{\cdot}30 < P < 0{\cdot}50$ (Table 5).

TABLE 5.—NUMBER OF INDIVIDUALS SMOKING STATED NUMBER OF CIGARETTES DAILY, WITH ALCOHOL CONSUMPTION MATCHED

Alcohol consumed (ml.)		*Number of cigarettes daily*				*Smoking habits Tb group versus controls*
		0-9	*10-29*	*30+*	*Totals*	
Nil ..	Tb group	5	3	3	11	$x^2 = 4{\cdot}88$, $n = 2$, $0{\cdot}1 > P > 0{\cdot}05$
	controls	13	19	2	34	
1-50 ..	Tb group	8	22	4	34	$x^2 = 0{\cdot}94$, $n = 2$, $P > 0{\cdot}50$.
	controls	14	29	10	53	
51-100..	Tb group	4	18	10	32	
	controls	1	7	3	11	$x^2 = 0{\cdot}12$, $n = 2$, $P > 0{\cdot}90$.
101+ ..	Tb group	1	13	9	23	
	controls	0	1	1	2	

$x^2 = 5{\cdot}94$. $n = 6$. $0{\cdot}30 < P < 0{\cdot}50$.

In contrast, when the tuberculous group and controls are matched according to tobacco smoked, there is still an excess number of the heavier consumers of alcohol in the tuberculous group. The difference is highly significant: $x^2 = 43{\cdot}60$, $n = 8$, $P < 0{\cdot}001$ (Table 6).

TABLE 6.—NUMBER OF INDIVIDUALS CONSUMING STATED QUANTITIES OF ALCOHOL, ML/DAY, WITH SMOKING HABITS MATCHED

Alcohol consumption ml. daily

Cigarettes daily		*Nil*	*1-50*	*51-100*	*101+*	*Total*	*Smoking habits Tb group versus controls*
0-9	Tb controls	5	8	4	1	18	$x^2 = 5{\cdot}43$, with two columns amalgamated, $n = 2$, $0{\cdot}1 > P > 0{\cdot}05$.
		13	14	1	0	28	
10-29	Tb controls	3	22	18	13	56	$x^2 = 27{\cdot}80$, $n = 3$, $P < 0{\cdot}001$.
		19	29	7	1	56	
30+	Tb controls	3	4	4	9	20	$x^2 = 10{\cdot}37$, $n = 3$, $0{\cdot}02 > P > 0{\cdot}01$.
		2	10	3	1	16	

$x^2 = 43{\cdot}60$. $n = 8$. $P < 0{\cdot}001$.

It appears that of the two conditions studied, smokers are in excess amongst tuberculous patients merely because heavy drinkers are likely to be heavy smokers. The relationship between tuberculosis and alcohol is more direct and is independent of smoking habits.

Quantity of Alcohol consumed related to the Incidence of Tuberculosis

Retrospective data, of the kind presented in Table 1, do not portray the incidence of tuberculosis as related to the amount of alcohol consumed. Doll and Hill (1952), when dealing with a similar problem, successfully applied retrospective data to statistics of population to estimate the incidence of lung cancer according to the amount of tobacco smoked.

The same technique has been applied to the present survey. Strictly, this can be applied accurately only to the ex-servicemen and not to the whole population for which figures are more easily obtained, but as the retrospective data, not the population figures, determine the relative rather than the absolute incidence of tuberculosis according to alcohol consumption, it is immaterial which population is examined.

There were 818,100 Victorian men between the ages of 20-69 years on December 31, 1958, 408 of them developed tuberculosis during the financial year 1958-59. Using the alcohol consumption of the controls, the total number of Victorian males consuming various quantities of alcohol has been calcu-

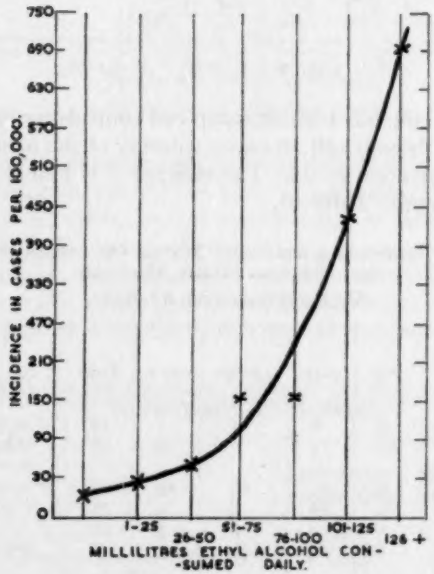

Fig. 1. Approximate incidence of tuberculosis in relation to the amount of alcohol consumed daily.

lated. Similarly, by using the drinking habits of the tuberculous sample, the numbers of the Victorian tuberculosis cases consuming various quantities of alcohol has been obtained.

From these two sets of figures the annual incidence of tuberculosis according to alcohol consumption has been estimated. The estimates charted in Fig. 1 may be regarded as approximations only, nevertheless they are useful to indicate an important trend. Light drinkers have only a slightly higher incidence of tuberculosis than non-drinkers, the incidence of tuberculosis is more obviously increased in moderate drinkers, and increases to an extraordinary extent amongst heavy drinkers.

Validity of Results

The tuberculous patients in Victoria were consecutive admissions and the controls were unselected admissions to the surgical wards of the hospital. Both groups were ex-servicemen of similar age distribution, with the exception of an excess of tuberculous patients between the ages 50-59 years, balanced by an excess of controls over 60 years (Table 7). This slight age dissimilarity is unimportant.

Table 7.—Age Distribution of Tb Group and Controls

Age in years	*Controls*	*Tb group*
20-29	5	4
30-39	27	25
40-49	21	24
50-59	13	28
60-69	27	16
70+	7	0
Unspecified	—	3
Total	100	100

The questionnaire was designed to be anonymous to allow a frank statement of smoking and drinking habits. With the voluntary participation of both tuberculous patients and controls, it was anticipated that the declared consumption of cigarettes and alcohol would be reasonably reliable. Minor inaccuracies no doubt occurred. Even so, these would be as likely to occur in either group and so would not cause a wide divergence between the tuberculous group and the controls.

Some confidence in the reliability of the description of the smoking habits is provided by the similarity between the results obtained in both Queensland and Victoria. Also, by estimating the alcohol consumption of the Australian male population the approximate correctness of the drinking habits of the controls can be tested.

The annual consumption of alcohol in Australia is 2·07 gallons per person aged over 15 years (Mackay, 1959). This equals 26 ml. ethyl alcohol daily.

This figure is obtained from sales of alcohol and consequently makes no allowance for subsequent breakages and spillage, etc. When allowance is made for wastage, the actual consumption would be rather lower than 26 ml.

As consumption in men is higher than that in women the consumption of men alone will be higher, probably in the region of 35 ml. daily.

This estimate is somewhat higher than 23 ml. daily, the average consumption of the controls. However, the controls were a rather elderly group with 34 per cent. over the age of 60 years. Slight allowance has to be made for the age composition of controls bringing the average consumption closer to the estimated figure. It is possible that the controls may have slightly understated their true consumption of alcohol. The degree of understatement is obviously too small to have caused the difference between the controls and the tuberculous group. Moreover, any understatement on the part of the controls is likely to have been shared by the tuberculous group.

That the high consumption of alcohol amongst the tuberculous group was a valid observation was supported by the number of known heavy drinkers in the group whose habits had been either openly admitted or disclosed by their subsequent behaviour.

For these reasons, it is believed that the results are a trustworthy indication of the major differences between the tuberculous group and the controls.

Discussion

Although the present investigation has confirmed the findings of Lowe (1956) that tuberculous patients smoke more heavily than controls, we have been unable to show that smoking is directly linked with tuberculosis. Rather, smoking was found to be linked with alcohol consumption, confirming the observations of Cartwright *et al.* (1959). Of the two factors, alcohol and not tobacco appears to be independently linked with tuberculosis. Previous investigations have demonstrated a high incidence of tuberculosis amongst alcoholics, Warnery *et al.* (1959), defining alcoholism as a daily consumption of 100 ml. of alcohol, found 183 alcoholics amongst 382 men admitted to a French sanatorium.

Kérambrun *et al.* (1959) found a consumption of 200 to 300 ml. of alcohol in 45 per cent. of tuberculous patients before their entry into another French sanatorium. Jones *et al.* (1954) reported the high incidence of tuberculosis amongst " Skid Row " alcoholics. Of the inmates of a Salvation Army Social Services Centre, 70 per cent. of whom were alcoholics, 2·2 per cent. were found to have tuberculosis, fifty-five times the rate for the general population of the same city. Fergus and Jackson (1959) discuss the high incidence of tuberculosis amongst alcoholics, and Ottenberg (1950) found 18 cases per 1,000 of tuberculosis amongst men jailed for drunkenness.

In the present study the results suggest that it is not merely the alcoholic but a wider class of alcohol consumer who have an increased incidence of tuberculosis. The association of tuberculosis and alcohol was not restricted to any particular group of drinkers, and all levels of alcohol consumption were associated with an altered incidence of tuberculosis.

From this and previous studies, it is difficult to decide whether the relationship between tuberculosis and alcohol consumption is a direct causal one or whether other factors link the two together. Vitamin or other deficiency commonly produced by heavy alcohol consumption is likely to favour the development of tuberculosis, as may the type of life led by a heavy drinker. Therefore there is good reason to suspect alcohol consumption as being an indirect causal factor. Moreover, there is experimental evidence that during alcoholic intoxication the emigration of phagocytic leucocytes in response to the presence of bacteria in the tissues is almost completely inhibited (Pickrell, 1938.) Even highly immunised animals develop septicæmia and succumb to a pneumococcal infection which non-intoxicated controls localise without the development of septicæmia, and survive. This effect of alcohol may operate to the disadvantage of persons harbouring tubercle bacilli.

If further work establishes unequivocally that alcohol consumption is a direct or indirect cause of tuberculosis, the problem of controlling the disease will be linked with the problem of controlling excessive alcohol consumption in the community.

From a public health aspect, case-finding is likely to be most fruitful if efforts are made to X-ray all heavy alcohol consumers. X-raying of the regular clientèle of all hotels would obviously be a promising new approach. This is not merely a question of X-raying derelicts, but all regular consumers of alcohol.

For the individual with tuberculosis, treatment should include an attempt to reduce the alcohol intake when this has been high.

Summary

On examining the tobacco and alcohol consumption of 100 tuberculous patients before diagnosis, and of controls, it was found that tuberculous patients were excessively heavy consumers of alcohol and, to a lesser extent, of tobacco. The tuberculous patients averaged the equivalent of nine 7-ounce glasses of beer daily compared with three glasses by the controls. Heavy smoking and heavy drinking were found to be linked together independently of tuberculosis. When the alcohol consumption of the tuberculous group and the controls was matched there was no difference between the smoking habits. In contrast, alcohol consumption was found to remain excessive when the smoking habits were matched. Thus, of the two habits, alcohol and not smoking was more directly associated with tuberculosis. The incidence of tuberculosis appeared to increase with the amount of alcohol consumed.

Although the present investigation cannot be regarded as proving that the relationship between alcohol and tuberculosis is causal, the results indicate that case-finding amongst heavy drinkers would be profitable and suggest the need for further investigation of the effect of the drinking habits of a community upon the incidence of tuberculosis.

We wish to thank Professor Douglas Gordon, Miss M. Daly, Miss E. Larson and Mr. T. G. Lithgow of the Queensland University for their assistance in obtaining the smoking habits of

the controls in Queensland, and Mr. K. J. Millar for assistance in obtaining the controls in Victoria. We are grateful to Mr. D. H. Shrapnel for the figure, and to the chairman of the Repatriation Commission for permission to publish this paper.

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Brit. J. Dis. Chest (1961) 55, 159.

Rare and Interesting Cases

TRAUMATIC DIAPHRAGMATIC HERNIA DUE TO A STAB WOUND OF THE CHEST

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Penetrating wounds of the diaphragm are the most frequent cause of traumatic diaphragmatic hernia (Jos, 1956). Indirect trauma from crushing of the chest or abdomen in motor-car accidents or falls from a height is the next most common cause. Post-operatively hernia may arise after incision of the diaphragm. Some penetrating wounds seem to be of minor importance and may thus be ignored. Strangulation is a serious complication and diaphragm raised by pregnancy may be injured by a small knife even in a relatively high wound.

Case Report

Mrs. R.D., a 25-year-old housewife, who was six months pregnant, was admitted to hospital on June 11, 1960. Two hours before admission, she had been stabbed with a penknife in the left lower chest. On examination her general condition was good and there was a stab wound about 1·5 inches long overlying the 8th left rib in the scapular line. Her chest was X-rayed (Figs. 1 and 2) and the wound was sutured in the casualty department. Soon afterwards she became increasingly breathless and there was some surgical emphysema around the wound. An intercostal tube was therefore introduced through the wound and it was connected to a waterseal drain. This considerably improved her breathlessness, but next day she complained of increasing pain in her chest, she vomited frequently and was dyspnœic. A Ryle's tube was passed and an emergency operation was performed on June 12, 1960. The lung was lying crumpled up in a corner and much blood was aspirated. Almost the whole stomach was lying in the chest; it was dusky in colour and had entered the chest through an incised wound in the dome of the diaphragm. The diaphragmatic incision was enlarged and the stomach was untwisted on its long axis; this improved its colour. It was then returned to the abdominal cavity and other abdominal viscera were found to be unharmed. The lower lobe of the lung was lacerated in three places; these injuries were repaired. The diaphragm was also repaired with a double row of silk sutures.

The post-operative course was very stormy, ileus persisted for several days. The patient developed repeated pulmonary atelectasis. After a week her general condition improved. She was delivered of a normal healthy child on September 4, 1960. Six months after her operation the patient was well and had no symptoms.

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Discussion

The first two cases of diaphragmatic hernia were reported by Ambroise Paré in 1610, both were from wounds. Another case, due to a stab wound, was reported by Fabricius Hildamus in 1646. Ashley Cooper's famous work on hernia appeared in 1824. He divided diaphragmatic herniæ into congenital and acquired groups, and the acquired group into those that passed through points of anatomical weakness and those which were traumatic. This classification has never been improved upon. Bowditch in 1853 collected 88 cases and added one from his own experience, but accurate diagnosis and understanding of diaphragmatic hernia awaited the discovery of Roentgen ray. In a series of 28 cases of traumatic herniæ, Hughes and his associates (1948) found that 17 were due to penetration and 11 caused by rupture of the diaphragm. Because of the splinting action of the liver the right side was less commonly affected. Although Hedblom (1934) said that 95 per cent. were left-sided, Hughes (1948) reported 5 on the right and 23 on the left. The hernia may not be obvious immediately after injury but may develop later; this occurred in 5 of Hughes's cases; one herniated 13 months after injury. Wolma *et al.* (1960) reported 3 cases in which there were late complications due to stab wounds of the diaphragm. In Hamdi and Sturdy's cases (1953) the herniation occurred because of the patient's straining while under anæsthesia for suture of other traumatic injuries.

Strangulation is a dangerous complication, and of 43 cases of herniæ with strangulation Carter *et al.* (1951) found that 34 occurred through trauma, 4 were congenital and 5 of unknown origin. Skinner *et al.* (1958) reported 10 patients having strangulated diaphragmatic hernia over a period of ten years; 4 of whom died after surgery: mortality of 40 per cent.

Traumatic hernia may be divided into those due to direct and those due to indirect injury. Indirect trauma is usually associated with crushing injuries and may produce a defect of any portion of the diaphragm. Direct trauma is due to penetrating wounds, *e.g.* gunshot or stab wounds. Traumatic rupture (indirect trauma) is met with more frequently on the left side than on the right. The rupture may be small and in the periphery of the diaphragm or it may be large and irregular in shape. It may often extend completely across the diaphragm into the œsophageal hiatus.

In a high percentage of cases obstructed or strangulated herniæ are traumatic in origin. In order of frequency the following abdominal viscera have been found passing through the opening in the diaphragm: 1. the stomach or part of it; 2. the greater omentum; 3. varying lengths of small intestine; 4. the transverse mesocolon; 5. the ascending colon and cæcum. In Pearson's case (1953) only the spleen and descending colon were in the peritoneal cavity. Though small and large bowel strangulate more readily than the stomach, the latter is not immune. A portion of stomach, frequently involved in diaphragmatic herniæ of both traumatic and non-traumatic origin, may strangulate by rotation on its long axis. Hamilton and Phillips (1949) reported 2 cases of traumatic hernia where the stomach became gangrenous due to torsion, and

FIG. 1.—P.A. view of chest soon after admission. Demonstrating an air-containing loculus above the level of the diaphragm and the collapsed left lung.

FIG. 2.—Lateral view of chest soon after admisson. Demonstrating the intrathoracic stomach.

To face p. 160

the present case also illustrates the vulnerability of the stomach to torsion and strangulation. The diagnosis of this complication is always difficult unless the possibility of an intrathoracic loculus of stomach is considered (Fig. 1).

Summary

A case of diaphragmatic hernia, soon after a stab injury of chest with a penknife in a pregnant patient is described. There was strangulation of stomach and lacerations in the lung. The release and untwisting of stomach restored its viability. She delivered normally at full term.

The literature on traumatic diaphragmatic hernia has been reviewed.

I am specially indebted to Dr. K. C. Pandey, D.A., for skilful anæsthesia in this case.

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GYNÆCOMASTIA AND BRONCHIAL CARCINOMA

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Bronchial carcinoma may be complicated by certain systemic or peripheral changes which have not resulted from local tissue destruction by the primary tumour or its metastases. The mode of production of these remote effects is obscure, as, for instance, in the rare complication of gynæcomastia. In previous case reports of this condition, mainly in the French literature, endocrine studies have been largely omitted. It is hoped that an account of a more fully investigated case, with details of hormone estimations, might therefore be of interest.

Case Report

The patient, a retired confectioner born in 1892, was first admitted to hospital in January 1958 complaining of a productive cough and increasing shortness of breath for the previous ten days. There had been no hæmoptysis or chest pain and no past history of chest illness.

On examination he appeared in good general condition. There was slight dyspnœa at rest, minimal finger clubbing, the right half of the chest moved poorly, was resonant to percussion, and the breath sounds were diminished over the whole of the right side.

The chest X-ray revealed a large pneumothorax on the right and an electrocardiogram showed atrial fibrillation. 1,200 ml. of air was aspirated from the right pleural space and ten days later a pleurodesis was performed with 10 ml. of ½ per cent. camphor in olive oil. Subsequent X-rays taken after the lung had re-expanded showed a previously unsuspected shadow at the right hilum which was strongly suggestive of a bronchial carcinoma. The patient refused to undergo bronchoscopy and discharged himself from hospital.

During the next two years there was no change in the chest X-ray and no new symptoms. In May 1960, just over two years after the original admission, he developed a productive cough, shortness of breath, hoarseness and dysphagia, and it was at this time that he first noticed a tenderness and swelling of both breasts. On examination the patient appeared ill but not emaciated. No abnormal pigmentation was seen. There was marked bilateral gynæcomastia, both breasts being tender. The testicles and prostate were normal size, the axillary and pubic hair were sparse. Several hard glands were palpable in the neck and the right external jugular vein was distended. There was slight finger clubbing, the trachea was deviated to the left, percussion note and breath sounds were diminished over the right upper lobe. There was a right-sided Horner's syndrome and marked dyphonia, indirect laryngoscopy showing paralysis of the right vocal cord.

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Investigations

Hb. 14·8 G/100 ml. W.B.C. 7,500 per cu. mm.

Serum bilirubin 0·7 mg./100 ml. Serum alkaline phosphatase 15·4 K.A. units/100 ml. Thymol turbidity 1 unit. Bromsulphthalein test, 3 per cent. retention in blood after 45 minutes. Hogben test, negative.

	Hormone assays/24 hour urine	
	1	*2*
17-Ketosteroids	8·2 mg.	12·8 mg.
17-Hydroxycorticosteroids	20·6 mg.	21·4 mg.
Œstrone	7·8 μg.	9·2 μg.
Œstradiol	4·7 μg.	5·7 μg.
Œstriol	22·4 μg.	23·1 μg.
Total œstrogens	34·9 μg.	38·0 μg.

The assay of œstrogens was performed by Dr. I. F. Sommerville, using a modification of Brown's method (Brown *et al.*, 1957), and the results showed three times the normal values for men. The chest X-ray showed a large dense opacity at the right hilum, enlarged right paratracheal lymph glands and multiple smaller opacities throughout both lung fields. Bone X-rays showed slight periosteal thickening at the lower ends of both tibiæ.

Biopsy of a cervical gland revealed a poorly differentiated squamous-cell carcinoma. The patient was treated symptomatically and he died three months later, two and a half years after presenting with a pneumothorax.

Necropsy Report

The body was of a thin old man. Both breasts were enlarged and consisted of mature glandular tissue with secretion in the lumina and a fibrous stroma containing moderate numbers of round cells. There was a large mass of carcinomatous tissue at the hilum of the right lung and widespread deposits throughout both lungs; it was not possible to determine the exact site of the primary growth, which had also spread into the superior mediastinum and neck. The pituitary gland appeared normal, but the adrenals and thyroid gland were both largely replaced by tumour tissue. The testes appeared normal with mitosis occurring in the seminal tubules, although there were few mature spermatozoa. Several small metastatic deposits were present in the liver, kidneys, spleen and cerebral hemispheres. The histological appearance of the tumour tissue was that of a poorly differentiated squamous-cell carcinoma.

Discussion

The case of bronchial carcinoma described was unusual in several respects. First, the presentation as an apparently simple spontaneous pneumothorax without other signs of pleural malignancy; secondly, the period of survival without treatment, two and a half years from the time of presentation; and, thirdly, the gynæcomastia, which is a rare complication.

Gynæcomastia is a term applied to enlargement of the breasts in males from hyperplasia of the glandular tissue and supporting stroma. The histological appearance, which is the same whatever the cause of the condition, closely resembles that of the developing female breast at puberty, when œstrogens are thought to provide the stimulus for growth (Hall, 1960).

In this case the concentration of œstrogens in the urine was three times the normal. In men the only glands that secrete œstrogens are the adrenal cortex and testes, and it is possible that either gland might increase its secretion so as to cause gynæcomastia. Several cases of bronchial carcinoma have been described with clinical features of adreno-cortical overactivity, usually with Cushing's syndrome, in which the excretion of 17-hydroxycorticosteroids was raised. At necropsy there was marked hyperplasia of the adrenal cortex with no metastases (Allott and Shelton, 1960). If a bronchial carcinoma can, in some cases, cause increased secretion of adrenal gluco-corticoids, it is conceivable that in others it might bring about an increase of adreno-cortical œstrogens. This seems unlikely in the case described, in which both adrenals were largely destroyed by metastases. Neither is it likely that the histologically normal testes were selectively stimulated to secrete excess œstrogens, with the 17-ketosteroid excretion remaining unchanged.

Although gynæcomastia is a well-known manifestation of chronic liver disease, resulting from defective hepatic breakdown of œstrogens, this defect could hardly have occurred in this case in which the liver function tests were normal and the post-mortem liver appeared almost free of metastases.

Perhaps the most acceptable suggestion is that the tumour tissue was itself producing œstrogenic hormones despite the fact that histologically it appeared to be a typical squamous-cell carcinoma. The concept of an œstrogen secreting tumour causing gynæcomastia accords well with the observation that in certain cases there has been almost immediate regression of breast changes following resection of the primary lung tumour (Fischl, 1950; Hardy, 1960). More surprisingly, in another patient a similar regression followed vagotomy (Huckstep and Bodkin, 1958).

In the case reported, the onset of gynæcomastia occurred two years after the carcinoma was first seen on an X-ray, at the stage when this hitherto relatively benign tumour first showed clinical signs of malignancy. Presumably at that time there was a change to a more anaplastic cell type, and the accompanying changes in cell metabolism might have resulted in the chance production of œstrogens. If this was the case, it is difficult to explain why such a very small proportion of tumours undergo this change.

Summary

The case of a patient with bronchial carcinoma is reported who presented with a spontaneous pneumothorax, and two and a half years later developed gynæcomastia. It is suggested that terminally the tumour may have become œstrogen secreting.

I should like to thank Dr. C. A. Young for permission to report this case, Dr. A. Jacobs for the post-mortem findings, and Dr. I. F. Sommerville of the Chelsea Hospital for Women, for performing the œstrogen assays.

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REVIEWS OF BOOKS

Proceedings of the Pneumoconiosis Conference, 1959. Edited by A. J. Orenstein. London: J. and A. Churchill. 1960. Pp. 632. 120s.

The proceedings of this Conference convened by the South African Council for Scientific and Industrial Research may be divided into three main headings. They are: (1) Engineering and Dust Sampling; (2) Clinical, Physiological and Radiological; and (3) Pathological. Eighty papers by expert contributors from Europe, South Africa and the U.S.A. are published.

There are interesting articles giving some modern views on the immunological approach to the causation of silicosis and biochemical findings in experimental animals. The apparent association in South Africa of Mesotheliomas of the pleura following long exposure to asbestos is described. There is no mention of a high incidence of frank bronchial carcinoma in patients with asbestosis as is recognised in this country.

The discussions, which must have been interesting, following these papers are reported in a rather disjointed manner.

K. F. W. Hinson.

Transactions of the 19th Conference on the Chemotherapy of Tuberculosis held February 8-11, 1960, Cincinnati, Ohio, by the Veterans Administration—Armed Forces, with the co-operation of the National Tuberculosis Association.

All who work in the field of chest diseases will be familiar with these transactions. Each volume grows thicker and the subject matter ranges more widely. The title does not do the contents justice, since fungal diseases of the lungs, emphysema and bronchitis, chemotherapy in bronchial carcinoma and a variety of other topics are also discussed. The Veterans Administration and Armed Forces Hospitals are often associated with teaching and other large private and municipal hospitals, so that the total clinical material is enormous, and trials of new drugs and combined therapies are possible on a large scale. These alone would make the Transactions worth reading. Particularly valuable are the papers on steroid therapy in tuberculosis, the long-term results of treatment of tuberculous meningitis, high *versus* low dosage of isoniazid, prognosis in the "open negative" case, radiological and cytological screening for lung cancer. Obviously the papers of so many contributors must vary in value, but the verbatim reports of the discussions often suffer from too careful transcription, and a little editing might improve their readability and detract little from their apparent spontaneity. At last we learn that bronchial infection is being considered in the U.S.A., even outside a few enlightened centres, as having some bearing on the ætiology of emphysema, and there is a short study of prophylaxis with antibiotics. The protocols of current and projected trials and studies are especially interesting, and may also guide potential visitors to America to the places where these are being carried out.

L. J. Grant.

Techniques of Thoracotomy. By B. T. Le Roux. Edinburgh: E. and S. Livingstone. Pp. 90. 65 Illus. 55s.

This volume presents the methods of approach to the thoracic and upper abdominal viscera which are practised in the Regional Thoracic Surgical Unit

in Edinburgh. There are numerous illustrations produced by the Medical Photography Unit of the University of Edinburgh.

It is perhaps unfortunate that the text is confined to the methods used in one clinic; by a slight extension it could have embraced all techniques of thoracotomy. One misses, for instance, a description of the prone position for thoracotomy, popularised by Sellors and still used by many surgeons. In the ninety pages of text attention is given to every conceivable detail of opening and closing the chest, even to extensive descriptions of the arrangement of the towels around the operation site. Whether this degree of detail is necessary is debatable. Of the sixty-five figures in the text, many are in colour, often containing four photographs. While some of the illustrations make their point well—for example, those dealing with open drainage of an empyema—the majority of those in colour are unsatisfactory. Even with a knowledge of the detailed anatomy of the chest wall it is frequently difficult to make out what the illustrations purport to show. Admittedly the thoracic wall does not lend itself to clear photography, but one cannot help feeling that artists' drawings, of the type so frequently seen in American textbooks, would have been a much more effective way of presenting the material, and would probably have reduced the cost of production. For its size, this is an expensive book, and while it contains a large amount of useful practical information the illustrations must weigh against its value.

GORDON CRUICKSHANK.

Respiratory Physiology and its Clinical Applications. By J. H. KNOWLES. Harvard University Press; London: Oxford University Press. Pp. 256. 42s.

This introduction to the subject is intended for the medical student and practising physician. It deals briefly with all the topics of normal and abnormal lung function and their investigation. The special clinical problems of lung disease and of diseases of other organs which disorder lung function receive individual attention. The more experienced reader will find it useful as a source of references: all the major and most of the minor problems of disordered respiratory function are mentioned in it and the bibliography is excellent. The use of each of the lung function studies is discussed. The presentation is informative rather than scientifically vigorous. The reader is not warned that some of the tests described might be less useful than was claimed by their originators, and that there may be simpler and equally valuable lines of investigation. This criticism, which can be levelled at every book on the subject of respiratory physiology, is made because " clinical application " appears in the title. It is a most useful primer.

L. CAPEL.

Cardiac Problems. Papers read at three symposia. London: The Chest and Heart Association. Pp. 144. 18s. 6d.

This small book gives proof that when a description of any clinical condition has to be abbreviated it very often gains in value, for here 18 authors deal succinctly with 17 different subjects in cardiology within the compass of 144 pages. It can be read within a few hours, and no clinician should be without the knowledge contained in this delightful little handbook.

WILLIAM EVANS.

A Synopsis of Children's Diseases By JOHN RENDLE-SHORT. Third Edition. Bristol: John Wright. Illus. 42s.

A critic's job in reviewing a synopsis is difficult. They are unreadable in a consecutive way, and it is only possible therefore to use them as a reference work. For this, Dr. Rendle-Short's book has an obvious use. It is certainly concise and contains much accurate information in readily available form. The index which is the key to a book of this sort is good, one finds what one wants with ease, but on occasion the search is fruitless. In such a common condition as talipes is it fair to find " see orthopædic textbooks "? There is a little too much of this and the only other fault is lack of reference to original papers despite the fact that many have been added since the last edition.

R. E. BONHAM CARTER.

Respiration. By P. H. ROSSIER, A. A. BÜHLMANN and K. WIESINGER. Edited by P. C. Luschinger and K. M. Moser. London: H. Kimpton. Pp. 505. 118s.

The American adaptation of this fine German textbook was carried out in close co-operation with the German authors. It presents a balanced view of the best work in the German and English languages. The four parts deal with the normal physiology of respiration, investigation of pulmonary function, the pathophysiology of respiration and pulmonary insufficiency in clinical practice.

The advances of modern respiratory physiology have depended on the application of physical and mathematical principles to medical problems. This is reflected in the text. Where a mathematical statement is required it is given simply and clearly.

The whole range of the clinical problems of disordered lung function is presented in the appropriate clinical and functional terms. Historical and early work is mentioned in perspective with the latest work. The bibliography is ample and up to date. Style, presentations and illustrations are excellent. This book presents a medical subject scientifically, but in a way well within the grasp of the physician. There is not a better serious account of the subject in one book.

L. CAPEL.

BOOKS RECEIVED

Surgical Diseases of the Chest. Edited by B. Blades. U.S.A.: C. V. Mosby Co.; London: H. Kimpton. 165s.

Conquering Your Allergy. By B. Swinny. London: Hammond, Hammond Co. Ltd. 12s. 6d.

Tobacco, Experimental and Clinical Studies. By P. S. Larson, H. B. Haag, and H. Silvette. America: Williams and Wilkins Co.; London: Baillière, Tindall and Cox Ltd. Pp. 944. 160s.

Treatment of Cancer and Allied Diseases Vol. 4. Tumours of The Breast, Chest and Esophagus. Edited by G. T. Pack and I. M. Ariel. London: Pitman Medical Publishing Co. Ltd. 650 illus. 240s.

Erratum

The publishers of the book *L'Hippocratisme Digital* reviewed in the January issue 1961 were incorrectly given as Masson et Cie. They are in fact J. B. Baillière et fils.

To face last page of text

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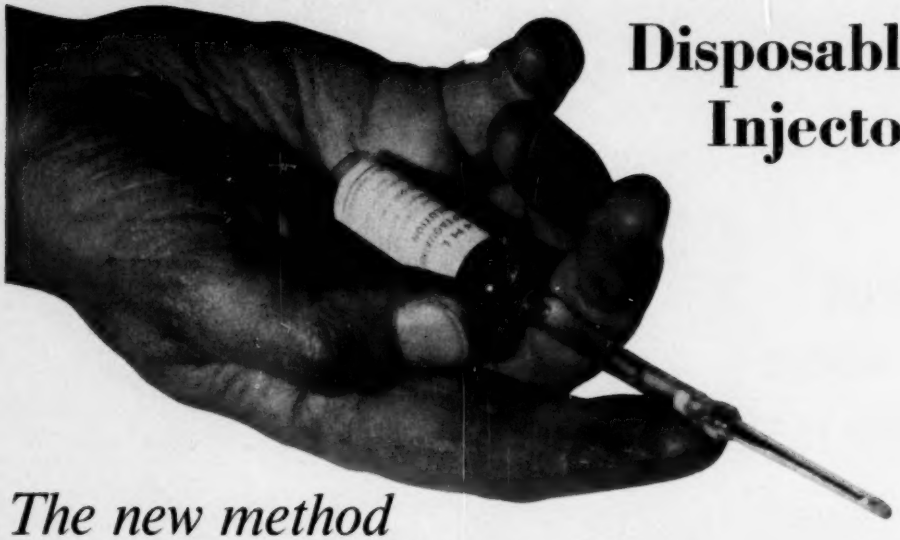

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